DOCUMENT RESUME

ED 144 327 EC 102 375

TITLE	Research on Disorders of the Mind. Progress & Prospects.
INSTITUTION	National Inst. of Mental Health (DHEW), Rockville, Md.
REPORT NO	DHEW-ADM-77-362
PUB DATE	77
NOTE	63p.; A meeting of the National Advisory Mental Health Council (100th, September, 1975)
EDRS PRICE	MF-$0.83 HC-$3.50 Plus Postage.
DESCRIPTORS	*Biological Influences; Conference Reports; *Drug Therapy; Emotionally Disturbed; *Genetics; *Psychopathology; Psychosis; Research Reviews (Publications); Schizophrenia; *Social Factors; Therapy

ABSTRACT

The 14 conference papers on mental illness focus on the biological, genetic, psychopharmacological, psychopathological, and epidemiological and social factors related to psychoses. Divided into five sections each preceded by a brief introduction, entries include the following titles and authors: "The Biological Substrates of Schizophrenia" (S. Kety); "The Psychobiology of Depression" (W. Bunney); "The Role of an Emergent Developmental Psychopathology in the Study of Vulnerability to Psychosis" (N. Garmezy); "Genetic Studies in Schizophrenia and Depression" (G. Winokur); "Analysis of the Impact of Phenothiazines and Related Drugs on the Treatment of Schizophrenia" (G. Klerman); "The Impact of Lithium on the Treatment of Manic-Depressive Disorders" (S. Gershon); "Pharmacological Research and the Psychoses--An Overview" (M. Lipton); "Psychopathological Factors in Psychoses" (M. Katz); "An Overview of the Psychopathology of Psychoses--Past, Present, and Future of the Biometric Approach" (J. Zubin); "Keys to Understanding and Treating Functional Psychoses" (J. Strauss); "Psychopathological Aspects of Psychoses--Nongenetic Factors in the Family Setting" (L. Wynne); "Social Factors Affecting Psychotic Behavior" (D. Mechanic); "Epidemiology and the Planning of Services for the Mentally Ill" (E. Gruenberg); and "Psychiatric Services and the Changing Institutional Scene" (M. Kramer). (SBH)

****
* Documents acquired by ERIC include many informal unpublished *
* materials not available from other sources. ERIC makes every effort *
* to obtain the best copy available. Nevertheless, items of marginal *
* reproducibility are often encountered and this affects the quality *
* of the microfiche and hardcopy reproductions ERIC makes available *
* via the ERIC Document Reproduction Service (EDRS). EDRS is not *
* responsible for the quality of the original document. Reproductions *
* supplied by EDRS are the best that can be made from the original. *
****

ED144327

U S DEPARTMENT OF HEALTH,
EDUCATION & WELFARE
NATIONAL INSTITUTE OF
EDUCATION

THIS DOCUMENT HAS BEEN REPRODUCED EXACTLY AS RECEIVED FROM THE PERSON OR ORGANIZATION ORIGINATING IT. POINTS OF VIEW OR OPINIONS STATED DO NOT NECESSARILY REPRESENT OFFICIAL NATIONAL INSTITUTE OF EDUCATION POSITION OR POLICY

013730

100th Meeting of the National Advisory Mental Health Council

Research on Disorders of the Mind:

Progress & Prospects

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Alcohol, Drug Abuse, and Mental Health Administration

National Institute of Mental Health
5600 Fishers Lane
Rockville, Maryland 20857

EC102375

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402

FOREWORD

This volume represents a review by outstanding scientists of the state of our knowledge about the serious mental disorders. Representing the spectrum of disciplines upon which study of the mind is based, prominent grantees and officials of the National Institute of Mental Health described their work before the 100th Meeting of the National Advisory Mental Health Council. The following chapters contain a somewhat revised and condensed version of the presentations. This volume is intended to serve as a source book for professionals and for laymen who devote themselves to the cause of the mentally ill.

Division of Scientific and Public
Information
National Institute of Mental Health
Rockville, Maryland

INTRODUCTION

Mental illness is a puzzle to which man has long sought the key. But the human mind is complex, and firm information about its workings has come slowly; solutions to the problems of mental disorder have been elusive. Recently, however, the long effort to understand the operation of the disordered brain has begun to yield results. Much progress has been made and more seems assured. There is a sense of optimism among many researchers about the possibility of at last finding definitive answers to the questions posed by mental disease.

The 100th meeting of the National Advisory Mental Health Council, held in September 1975, reflected this optimism. The meeting brought together leading scientists in the field for a full day of talk about the results and implications of 25 years of research on the causes and treatments of serious mental disorder. The record of the day's remarks provides both an overview of a remarkably productive period and a brief look at the promise of the years ahead.

The past quarter century has seen tremendous advances in the scientific knowledge about mental illness. At the time the Council was founded, little was known about psychoses that was really useful. We could describe such serious mental disorders as schizophrenia and depression—apparently they are as old as humankind—but we could not treat them with any assurance of success, and we understood very little about their connection with human biology.

Today our understanding is greatly expanded. We have clinical and epidemiological data that shed light on the nature, the incidence, and the course of serious mental disorder. We have treatments available, in the form of drug therapy, that make a significant difference in the management of psychoses. Most important of all, we have the beginnings of an understanding of the biological factors involved in mental illness. Biological investigation is today an accepted part of the basic research going forward on mental illness. Of all the changes over the last quarter century, it is this shift in the direction of biological research that is most revolutionary. From an almost entirely psychodynamic approach, research in the mental health field has expanded to include genetic and biochemical studies as a matter of course.

Several speakers discussed some of the pioneering studies in the biological aspects of psychoses and their effect upon the theory of mental illness. Though differently focused, these presentations had at least two points in common: First, each researcher stressed that the existence of biological variables in psychoses is no longer speculative, but incontrovertible. The proof is there in careful, rigorously conducted research. Second, all agreed that the information we now have, though it represents an enormous advance over the state of knowledge even a few years ago, is, as I have said, only a beginning. But it is a beginning full of promise. The in-

formation yielded thus far by genetic investigations, classification and population studies, and neurobiological research holds out the hope that further efforts in these and related areas will eventually provide us with an understanding of the basic physical mechanisms of mental disorder.

To say this is not to suggest, however, that cultural and social variables that also affect mental health can be overlooked. Several participants discussed these factors, pointing out the complex interrelationship that exists between the biological and the psychosocial aspects of psychoses.

The remarkable advance brought about by the discovery of psychotropic drugs for treatment of psychosis is another major accomplishment dealt with in this volume. The interplay between the empirical knowledge gained by using psychoactive drugs in the management of mental illness and the experimental efforts to discover the mechanisms by which they work has been extremely fruitful. The contribution of psychopharmacology to basic theoretical understanding of psychosis, as well as to improvement of patient care, has been and undoubtedly will continue to be of great importance.

The final area covered in this report deals with the epidemiology of psychoses. A review is made of the statistics—past, present, and future—on mental illness in the population of this country. All agreed that the number of persons suffering serious mental disorder has risen as longevity has increased, and that these numbers will continue to rise as a greater proportion of the population reaches old age. The implication of these figures for those of us concerned with mental health is clear: We are certainly a growth industry. Once again, the results of the studies of the last 25 years furnish us with urgent questions for the future. How will we meet the challenge of greater numbers of patients requiring mental health care? Are there preventive measures that will prove effective against psychoses? What is the role of families and of communities in mental health?

Taken as a whole, the picture presented at the 100th meeting is both exciting and optimistic. To be sure, there are the sobering statistics, and certainly there is recognition by researchers of the limits and problems of drug therapy. Every speaker, even as he outlined the accomplishments of the recent past, took notice of how much more we need to know. Although the mentally ill are much better off today than ever before, the fact remains that they still live in the shadows of our society. A fundamental change in their condition awaits the discovery of yet more pieces to the puzzle.

Yet the knowledge gained over 25 years of open-minded, open-ended research has brought us so far that it is possible to believe that, with time and continued effort, we will be able not just to ameliorate but to solve the problems of serious mental illness. All of us harbor the hope that solutions will be found in our time. Every mental health researcher wants to believe, as Dr. Garmezy has said: "The dawn of the 21st century may witness an end to the scourge of madness."

Bertram S. Brown, M.D.
Director
National Institute of Mental Health

LIST OF MEETING CHAIRMEN AND SPEAKERS

Bertram S. Brown, M.D., Director
National Institute of Mental Health
Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20852

William E. Bunney, Jr., M.D.
Chief, Adult Psychiatry Branch
Intramural Research Program
National Institute of Mental Health
National Institutes of Health
Bethesda, Maryland 20014

Daniel X. Freedman, M.D.
Professor and Chairman
Department of Psychiatry
University of Chicago
950 East 59th Street
Chicago, Illinois 60637

Norman Garmezy, Ph.D.
Professor of Psychology
Department of Psychology
University of Minnesota
Minneapolis, Minnesota 55455

Samuel Gershon, M.D.
Professor of Psychiatry
Director, Neuropsychopharmacology
Research Unit
New York University Medical Center
Building 550, First Avenue
New York, New York 10016

James A. Goodman, Ph.D.
Director, School of Social Work
University of Minnesota
Minneapolis, Minnesota 55455

Ernest Gruenberg, M.D., Dr.P.H.
Professor and Chairman
Department of Mental Hygiene
School of Hygiene and Public Health
The Johns Hopkins University
615 North Wolfe Street
Baltimore, Maryland 21205

Martin M. Katz, Ph.D.
Chief, Clinical Research Branch
Division of Extramural Research Programs
National Institute of Mental Health
Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20852

Seymour S. Kety, M.D.
Professor of Psychiatry
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts 02114

Gerald Klerman, M.D.
Professor of Psychiatry
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts 02114

Morton Kramer, Sc.D.
Director, Division of Biometry and
Epidemiology
National Institute of Mental Health
Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20852

Jerome Levine, M.D.
Chief, Psychopharmacology
Research Branch
Division of Extramural Research Programs
National Institute of Mental Health
Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20852

Morris A. Lipton, M.D., Ph.D.
Sarah Graham Kenan Professor of Psychiatry
Director of the Biological Sciences
Research Center
Child Development Research Institute
School of Medicine
University of North Carolina
Chapel Hill, North Carolina 27514

David Mechanic, Ph.D.
John Bascom Professor of Sociology
Director for Center of Medical Sociology and Health Services Research
University of Wisconsin
Madison, Wisconsin 53706

John S. Strauss, M.D.
Director, Clinical Psychiatry Research Programs
Department of Psychiatry
University of Rochester
School of Medicine and Dentistry
Rochester, New York 14642

George Winokur, M.D.
The Paul W. Penningroth Professor and Head
Department of Psychiatry
University of Iowa
Iowa City, Iowa 52242

Lyman C. Wynne, Ph. D.
Professor and Chairman
Department of Psychiatry
University of Rochester
School of Medicine and Dentistry
Rochester, New York 14642

Joseph Zubin, Ph.D.
Professor Emeritus (Psychology)
Special Lecturer in Psychiatry
Columbia University
722 West 168th Street
New York, New York 10032

CONTENTS

		Page
Foreword		iii
Introduction		
	Bertram S. Brown	v
List of Meeting Chairmen and Speakers		vii
I.	**BIOLOGICAL ASPECTS OF PSYCHOSES**	
	Daniel X. Freedman, Chairman	1
	The Biological Substrates of Schizophrenia	
	Seymour S. Kety	2
	The Psychobiology of Depression	
	William E. Bunney, Jr.	7
II.	**GENETIC FACTORS IN PSYCHOSES**	
	Daniel X. Freedman, Chairman	10
	The Role of an Emergent Developmental Psychopathology in the Study of Vulnerability to Psychosis	
	Norman Garmezy	11
	Genetic Studies in Schizophrenia and Depression	
	George Winokur	16
III.	**PSYCHOPHARMACOLOGICAL ASPECTS OF PSYCHOSES**	
	Jerome Levine, Chairman	19
	Analysis of the Impact of Phenothiazines and Related Drugs on the Treatment of Schizophrenia	
	Gerald Klerman	20
	The Impact of Lithium on the Treatment of Manic-Depressive Disorders	
	Samuel Gershon	22
	Pharmacological Research and the Psychoses: An Overview	
	Morris A. Lipton	24
IV.	**PSYCHOPATHOLOGY OF PSYCHOSES**	
	Martin M. Katz, Chairman	26
	Psychopathological Factors in Psychoses	
	Martin M. Katz	27
	An Overview of the Psychopathology of Psychoses: Past, Present, and Future of the Biometric Approach	
	Joseph Zubin	29
	Keys to Understanding and Treating Functional Psychoses	
	John S. Strauss	34
	Psychopathological Aspects of Psychoses: Nongenetic Factors in the Family Setting	
	Lyman C. Wynne	38

242-844 O - 77 - 2

Page

V. EPIDEMIOLOGICAL AND SOCIAL FACTORS IN PSYCHOSES
James A. Goodman, Chairman 45
Social Factors Affecting Psychotic Behavior
David Mechanic 46
Epidemiology and the Planning of Services for the Mentally Ill
Ernest Gruenberg 51
Psychiatric Services and the Changing Institutional Scene
Morton Kramer 53

I. BIOLOGICAL ASPECTS OF PSYCHOSES

During the past quarter century, one of the greatest achievements in the mental health field has been the recognition of a biological basis for serious mental disorders. Research has shown clearly that biological, along with environmental and sociological, factors affect the incidence and course of psychoses.

The importance of this achievement can hardly be overstated since it has opened up new ways of approaching every aspect of mental illness, from onset to treatment, from prevention to rehabilitation. It has linked science and the public as advocates for the neglected mentally ill, thereby reinforcing scientific concern for the mentally ill.

Biological research has answered many questions; it continues to raise new questions in the search for an understanding of the age-old problem of mental illness.

Daniel X. Freedman, M.D.

The Biological Substrates of Schizophrenia

Seymour S. Kety, M.D.

Schizophrenia is one of our major national health problems primarily because it affects people at a young age and causes constant or recurrent incapacity for meaningful and productive lives. In the previous generation, researchers in the young sciences of microbiology and biochemistry had discovered the causes of two other major mental illnesses—general paresis and pellagrous dementia—which by 1950 had practically disappeared. But schizophrenia has remained with us. Despite the fact that 20–40 million Americans will at some time in their lives be seriously handicapped by this illness, our knowledge about its causes has been woefully inadequate, and, therefore, we do not yet know how to prevent it. Over the past 25 years we have had a lot of opinions instead of knowledge and facts. We have had doctrinaire beliefs upon which major action was taken: ideas that schizophrenia was a simple disease of the brain and could be demonstrated at autopsy, ideas that schizophrenia was a nonspecific vitamin deficiency and could be treated effectively with huge doses of a potpourri of vitamins, the belief that biology had little to contribute to schizophrenia since the disease was caused by the way "schizophrenogenic" parents reared their children, or even, the idea that schizophrenia was not an illness at all but a creative adaptation to an evil society and that social mediation was the remedy for the disease.

Interestingly enough, the progress I have been fortunate enough to witness over the past 30 years was not made by those who thought they knew the answers in advance, but by those who were willing to admit they did not know and who spent their lives searching for knowledge that might eventually provide the answers. Progress was often achieved by those who contributed bits of knowledge that neither they nor anybody else realized was relevant to schizophrenia. Thirty years ago it was thought by some that schizophrenia was a circulatory disturbance of the brain and that, therefore, the brain was not getting enough oxygen. We had just developed a technique for studying the circulation and oxygen consumption of the human brain. Comparing 30 schizophrenic patients with normal young men, we found that there was no insufficiency of oxygen in their arterial blood, that their cerebral blood flow was within normal limits, and that the energy their brain utilized (measured in terms of oxygen) was exactly the same as in normal individuals. From this we concluded that it takes just as much oxygen to think an irrational thought as to think a rational one.

But we made another, more important, discovery. We realized that the brain is a marvelously more complex machine than any that had ever been devised. Most machines are dependent on their energy supply. The output of the brain under most circumstances has little to do with its energy utilization. It takes no more energy for a statesman to make a speech or a decision which would alter the course of history than it does for a fool to make an error. There are, of course, various types of coma in which the oxygen or energy supply is diminished, but as long as the power supply is maintained, the output of the brain in thought, feeling, and action is dependent on biological processes far more complex and subtle than its power supply. But 30 years ago we had not the vaguest idea of what those processes might be.

We established laboratories in the various biological and clinical disciplines that might pertain to mental illness and might contribute

ultimately to its understanding. We had no idea where the answers were going to come from; but, being fairly confident that they were going to come from many sources, we placed our bets evenly across the board, supporting all of the disciplines—the social, the psychological, and the biological—without trying to anticipate which were going to be the most important, in fact, not even feeling that one was more important than the other.

In time, a Laboratory of Clinical Science was organized. It attempted to bridge the gap between basic research and the clinical problems of mental illness, particularly those of schizophrenia. The laboratory addressed the hypothesis that schizophrenia was caused by an abnormal metabolic pathway in which epinephrine was oxidized to adrenochrome. That was supposedly a hallucinogenic substance that could produce some of the symptoms of schizophrenia. The difficulty in testing the hypothesis was that practically nothing was known about the metabolism of epinephrine in normal individuals, let alone in schizophrenics. So the first task was to learn more about its normal metabolism. As a result of work done by Julius Axelrod, our knowledge of the metabolism of epinephrine moved from almost complete ignorance to an ability to account for practically all of its metabolism in the body. This contribution permitted us to test the hypothesis that epinephrine metabolism was abnormal in schizophrenics.

We studied 12 normal individuals and 12 schizophrenic patients, and, as in the case of the cerebral circulation, the schizophrenics were exactly the same as normals. We found no evidence for the production of adrenochrome in schizophrenia.

Around that time, the generally accepted model of the human brain was that of the electronic computer with the body's sense organs translating the external world into electrical signals which were then processed through the complex circuits of the brain and either stored in memory banks or passed down to the muscles or glands, thus resulting in behavior. The only place where biochemistry was seen as operating in human behavior was in the oxidation of substrates that provided the energy for this complex circuitry of the brain. If that were indeed the model of human behavior, it was not likely that biochemistry would be able to make much of a contribution to the higher aspects of human thought and behavior. Coma and many types of mental retardation might have a chemical basis, but information transfer, mood, judgment, decisions, and rationality would remain dependent on the circuits of the brain and their electrical connections. It did not seem likely that a biochemist could unravel these circuits any more than he would be able to locate a faulty circuit in a computer. And if the trouble was in the information that had been fed to the computer, none of the biological sciences were likely to be of help.

However, there were some reasons to feel that the mental illnesses were not simple disturbances in information storage or input but that perhaps they represented some pervasive metabolic or biochemical disturbance that is reflected in the irrational thinking or the terribly depressed moods that characterize these illnesses. The evidence for that hypothesis came from studies which showed a familial distribution of mental illness, both schizophrenia and the affective disorders. It was well known that these disorders ran in families, and it was a common assumption that genetic factors were important.

However, that didn't prove the operation of genetic factors. Poverty runs in families, pellagra ran in families, and they are not genetic disorders. A family shares both its genetic endowment and its life experience, and a disorder that runs in a family could equally reflect the environmental influences as well as the genetic factors that its members share.

Then came twin studies that made the genetic evidence more crisp and more compelling. In monozygotic twins, who are genetically identical, schizophrenia very often affects both twins, whereas in dizygotic or fraternal twins, who are simply siblings conceived and born at the same time, schizophrenia usually affects only one. This evidence was suggestive, but it was still possible to point out that monozygotic twins share a great deal of their environment and that, therefore, one can't be sure that the

concordance for an illness like schizophrenia is not due to their ego identification or the many more environmental factors they have in common than do fraternal twins.

Recently, the definitive study on twins has been carried out by Irving Gottesman and James Shields, in which they have rectified most of the imperfections of the previous twin studies. They have clearly demonstrated, using several diagnosticians who read the case records without knowing who was the twin of whom, that there is an illness called schizophrenia, that psychiatrists can recognize it with considerable reliability, and that it is more often paired in monozygotic than in fraternal twins. But even that study could not randomize or hold constant the environmental influences. Thus there has been a loophole in the genetic evidence, and it must have been rather large since whole schools of psychiatry have marched through it.

Because of the inadequacy of the evidence, a group of us in the NIMH Program decided there was another approach to the problem that might finally disentangle the genetic and environmental influences in schizophrenia. That was the study of adopted individuals who have a biological family with whom they do not live but from whom they derived their genetic endowment, and who have an adoptive family not genetically related to them but with whom they have been reared and shared environmental influences. Over the past 13 years, David Rosenthal, Paul Wender, and I, with our collaborators in Denmark, notably Fini Schulsinger, have conducted studies on the total adopted population in that country who are now adults. We identified among them those who could be diagnosed as schizophrenic. We then traced their biological and adoptive relatives and examined them for evidence of mental illness on a blind basis, that is, without knowing their relationship or whether they were biological or adoptive relatives.

What we found in each of these studies was a familial tendency for schizophrenia—but only in the biological relatives of schizophrenics who shared their genes and not their environment. The adoptive relatives who have reared the probands and shared their life experiences show no higher prevalence of schizophrenia than the general population. It seems clear, then, that genetic factors must operate significantly in the transmission of schizophrenia.

These findings do not rule out environmental factors, and we believe the environmental factors are important. The task is to find what these environmental factors are. They may be social or familial in nature, but they could also represent such possibilities as infections, birth injuries, or dietary influences.

Genetic determinants of disease, whatever their nature, can only operate through biochemical processes. The past 25 years have brought an elucidation of what these processes may be. That period saw a dramatic growth in the neurosciences and an unprecedented development of knowledge regarding the brain and behavior. The 10 billion nerve cells of the human brain communicate with each other by way of complex switches known as "synapses." These, once thought to be electrical junctions, are now known to be chemical in nature, with chemical molecules (neurotransmitters) carrying the message. Since sensory processing, perception, thought, feeling, and behavior all depend on the operation of these switches, this discovery pinpointed the site at which chemical substances, metabolic products, hormones, and drugs could modify crucial aspects of the mental state and behavior. Biochemical disturbances in mental illness could be expected to have their effects at the synapse, and drugs that ameliorate these illnesses should also act there.

Although there are hundreds of billions of synapses in the human brain, they are organized in a marvelously systematic way along certain pathways that are being mapped by neuroanatomists. Several different types of neurotransmitters have been identified and found to be associated with different pathways, functions, and behavioral states. Considerable progress has been made in identifying the pathways and the transmitters that interact to produce disturbed mental states (in the areas of arousal, attention, rage, fear, motivation, and exhilaration) in the major psychoses. While these neurotransmitters were being discovered and

mapped in the brain, several drugs were discovered independently to exert specific and beneficial effects on disturbances of mood, thought, and behavior.

In 1950, chlorpromazine was found to be useful in the treatment of schizophrenia. This came about as a result of a large amount of research unrelated to mental illness on dyestuffs, organic synthesis, histamine, and the sympathetic nervous system; as a result of all of these, a compound was produced which antagonized histamine and also blocked sympathetic activity. An anesthesiologist in France who had some ideas about how to control surgical shock used chlorpromazine because of those actions. I am not sure he ever proved his hypothesis about shock, but he made an even more important contribution. He noticed a beatitude and tranquillity in those patients that seemed to be different from ordinary sedation, and he suggested to some of his psychiatrist friends that they might want to try it on mental patients. Chlorpromazine was found to be very effective in the treatment of schizophrenia, especially on its psychotic manifestations; no previous drug had ever achieved these results. The drug's properties were quickly recognized, and in a matter of 2 or 3 years chlorpromazine was used widely throughout the civilized world, thus revolutionizing the treatment of schizophrenia.

A new field of psychopharmacology emerged, bringing the newly acquired knowledge and techniques of neurobiology and behavioral science to bear on the mechanisms of action of these drugs. It has been found that all of the drugs that are useful against depression increase the concentration or the effectiveness of the monoamine transmitters at their synapses in the brain. Lithium, which dramatically relieves mania and is effective in preventing the recurrence of manic-depressive episodes, has been found to stimulate the synthesis of the neurotransmitter serotonin.

Not only did chlorpromazine and the drugs it engendered revolutionize the treatment of schizophrenia, it also broke the first path to the biological processes which underlie that disorder. In addition to its beneficial action, chlorpromazine had an important side effect: It produced in some patients facial and motor disturbances similar to those seen in Parkinson's disease. New drugs were developed in an effort to avoid these symptoms, but the therapeutic effect and the neurological side effect seemed to go hand in hand for some unknown reason. It took 10 years for the explanation to emerge.

In 1960, a technique was perfected in Sweden for identifying certain neurotransmitters in the brain by means of their characteristic fluorescence under appropriate conditions. A pathway which utilized the transmitter dopamine was discovered in the region of the brain that was known to be affected in Parkinson's disease. This led to the demonstration that Parkinson's disease was caused by a deficiency of dopamine in that region; the side effect could be effectively treated by the administration of dopamine's precursor, L-dopa. That represented one of the major contributions of fundamental research to the treatment of neurologic disorder. It also had important implications for psychiatry. Since the antischizophrenic drugs also caused symptoms of Parkinson's disease, the hypothesis was developed, tested, and validated that these drugs act to block the physiological action of dopamine at its synapses. In fact, there is an excellent correlation between the ability of each of these drugs to block dopamine and its efficacy as an antipsychotic agent. Interestingly enough, amphetamine, which acts in the opposite direction to stimulate dopamine synapses, can produce in individuals who abuse it a toxic psychosis that is indistinguishable from schizophrenia and can also be terminated by the antischizophrenic drugs.

Very recently, the first discovery of a genetic biochemical lesion producing a schizophrenic psychosis came from the Intramural Research Program of NIMH. Dr. Harvey Mudd, at NIMH, in collaboration with physicians at Johns Hopkins, studied a patient there who had been diagnosed by several psychiatrists as schizophrenic. She was also excreting large quantities of the amino acid, homocystine. This was identified as an unusual kind of homocystinuria resulting from a genetic deficiency of the enzyme, methylene tetrahydrofolate reductase. From the

basic research which he and others had carried out on that enzyme, Dr. Mudd realized that folic acid should be able to substitute for the action of this enzyme in the body.

When the patient was treated with folic acid, her schizophrenia disappeared, and she was discharged from the hospital. She stopped the treatment after a while and became schizophrenic again. This happened several times; each time, folic acid brought about the disappearance of her schizophrenic manifestations.

Obviously this does not explain schizophrenia because that enzyme defect is extremely rare, and folic acid is generally not known to help schizophrenics. It does suggest, however, that there may be a substantial number of different disorders that result in schizophrenia and that careful and imaginative research may uncover them one by one. Nor can we say today that the answer to schizophrenia lies in the dopamine, norepinephrine, or serotonin synapses of the brain. These are not the only chemicals transmitted; several more are known and more will be discovered. We also know that many other biological, psychological, and social factors interact with these systems.

It is fairly certain, however, that further research along the many paths that are now opened up will bring us a closer understanding of the chemical disturbances which form the biological substrates of these illnesses. And with that understanding will come, as it has in the case of other illnesses, more effective means for prevention and treatment.

The Psychobiology of Depression

William E. Bunney, Jr., M.D.

I would like to describe some of the research in the field of depression that has been completed during the past decade. I will present a general approach to the problem of affective illness together with some specific examples of research that has been conducted at the National Institute of Mental Health.

The prevalence of affective illness in the United States is estimated at four to eight million individuals. In the past few years, there have been major advances in the study of the genetics, diagnosis, and treatment of this major mental illness.

A new diagnostic category that seems to be particularly useful in terms of research and treatment divides the illness into two subgroups—the unipolar and the bipolar depressions. Unipolar patients have a history of recurrent episodes of depression. They experience feelings of hopelessness and worthlessness, have trouble sleeping, have black moods and thoughts of death and dying, and exhibit suicidal behavior. One of the most striking aspects of depressive illness is the intensity of the psychological pain the individual experiences. It is this psychological pain that is often manifested by suicidal attempts. The bipolar patient, on the other hand, fluctuates between mania and depression. Manic behavior includes flight of ideas; psychotic and grandiose thinking; bizarre, inappropriate behavior; destructive actions; and increased verbal and motor activity. The age of onset of the unipolar patients tends to peak at about 45, while the bipolar patient onset peaks at about 25. There is a lower incidence of mania in the relatives of unipolar patients and a higher incidence in the relatives of the bipolar patients.

Some of the genetic data relevant to affective illness include the findings that there is a higher incidence of mania in members of the same family than in the general population and that there is a higher incidence of mania in identical twins than in nonidentical twins. Five investigations that were conducted in three countries over a span of 15 years support the finding that if one identical twin becomes ill with affective illness, there is an approximately 70 percent chance that the other identical twin will become ill, while if a nonidentical twin becomes ill with affective illness, there is only about a 15 percent chance that the other nonidentical twin will also become ill. At present there are no definitive studies concerning affective illness of twins separated in early childhood and reared in different environments. Drs. Kety and Rosenthal and their collaborators are currently conducting studies of this type in Scandinavia. However, 12 cases have been reported in the literature of adults who were identical twins separated at birth and who have developed affective illness. Of these 12, the incidence of concordance was 69 percent.

The genetic data lead us to a way of conceptualizing the psychobiology of affective illness which is similar to that reviewed by Dr. Kety for schizophrenia. If genetic factors exist, they are probably expressed as a protein defect or abnormality. The depression or mania observed in affective illness can be activated by drugs and can be reversed by drugs. These compounds are probably activating or reversing a protein defect. The defect could be acquired in utero, at birth, or environmentally. It is probably genetically acquired. All of the compounds that activate or reverse these pathological conditions af-

242-844 O - 77 - 2

fect monoamine neurotransmitters in the brain. Thus it appears that this is a very critical area to investigate for a possible genetically transmitted protein defect in depression.

In attempting to study an illness scientifically, it is important to confine one's attention to a specific area. In collaboration with Drs. Frederick Goodwin, Dennis Murphy, and Robert Post, we have identified the "switch process." Bipolar patients often remain in a retarded depression for many months in which they are relatively mute, retarded, and dozing. Over the course of a few hours, they can "switch" into a hyperactive manic episode. It is hypothesized that this is due to a change in brain biochemistry and perhaps a change in the metabolism of neurotransmitters just prior to the onset of the switch. The number of switches that a patient may experience during a lifetime may vary. Some patients switch once or twice a year, while a few patients switch every other day between a severely retarded depression and an uncontrollable mania. A typical patient will be noncommunicative for 3 or 4 months and then will switch, over the course of 2 to 12 hours, from a nonverbal, retarded depression to a hyperactive, manic state. At the present time, we have studied 54 rapid switches in patients, and one of the most consistent findings is that the switch usually occurs during the night and that on the night prior to the switch, or the night of the switch, the patient has an absence of sleep.

At this point, it is important to comment briefly on the metabolism of the neurotransmitters in the brain because our further understanding of the manic-depressive process and of the mode of action of drugs which can activate or decrease manic and depressive symptomatology is dependent on knowledge gained from basic research. Nerve impulses are transmitted from one nerve ending to another by compounds called neurotransmitters. These compounds are made in the nerve ending, stored, and released; they then carry the message from one nerve to the other, react with the second nerve, and then the neurotransmitters are broken down or restored in the original nerve ending.

Drugs that affect each of the steps mentioned above are now available and their effects have been studied in man. A hypothesis suggests that mania is associated with an increase, in the brain, of the neurotransmitters norepinephrine or dopamine, and that depression is associated with a decrease. Therefore, drugs that increase norepinephrine or dopamine in the brain might be expected to activate mania or to activate the switch process, while drugs that decrease norepinephrine or dopamine in the brain would be expected to decrease mania.

Three compounds which increase these neurotransmitters in the brain have been clearly associated with the onset of mania. They include L-dopa, a compound from which one of the neurotransmitters is formed. L-dopa was given in large doses in an attempt to help depression. It was found that it often was associated with brief manic episodes. Similarly, two groups of compounds that are used to treat depression, the tricyclic compounds and the monoamine oxidase inhibitors, both increase brain norepinephrine by different mechanisms and have been associated with the sudden triggering of a manic episode in bipolar patients (those patients who have histories of both mania and depression). It is of interest that these compounds very rarely trigger mania in unipolar patients (those patients who have no histories of previous mania). This suggests a vulnerability to increased norepinephrine or dopamine in bipolar patients.

Evidence is also available that three compounds known to decrease the availability of brain norepinephrine or dopamine can decrease manic symptoms. The first is lithium carbonate, which has been shown in basic research on animals to decrease the release of norepinephrine and to increase its reuptake. This compound is particularly effective in decreasing mania, and the extreme sensitivity of patients to lithium was first shown at NIMH. It was found that if a patient receives a placebo rather than lithium for only 24 hours, he will have an exacerbation of the manic symptoms. Many patients with chronic manic-depressive illness have been helped with lithium. For example, one patient was a college student who had required hospital-

ization in a State hospital for 3 years prior to treatment with lithium. The patient has been essentially symptom-free for 10 years since, and has been able to complete college, to teach school, to marry, and to have a child. Another patient spent 10 years in a hospital prior to treatment with lithium. On lithium during the past 8 years, this patient has not required hospitalization.

A second group of compounds, the neuroleptics, block receptors for the neurotransmitter dopamine and also can decrease mania. Finally, a compound, alpha-methyl-para-tyrosine (AMPT), which specifically blocks the formation of the neurotransmitters norepinephrine and dopamine, was shown in an NIMH study to decrease mania in five of seven patients.

Compounds such as L-dopa and AMPT, which have specific effects on specific neurotransmitters, provide a great deal of rather powerful information concerning the possible causes of manic-depressive illness.

Thus we have reviewed three compounds that increase brain norepinephrine and dopamine and which have been associated with the triggering of mania in bipolar patients. We have also discussed an additional three compounds that decrease functional brain norepinephrine or dopamine and which have been shown to produce a remission in manic symptoms. This suggests that the neurotransmitters norepinephrine and dopamine may in some way be involved in the etiology or the modulation of serious manic symptomatology.

One new area under investigation at NIMH is the receptor for the neurotransmitter. It has been shown that drugs can increase or decrease the sensitivity of receptors to neurotransmitters. This is currently being explored; the possibility of altering receptor sensitivity prior to administering a standard antidepressant drug could present a new research strategy that might decrease the usual 2 to 3 weeks required for the current antidepressants to act. This development is very important clinically since it is during this time that the patient may be most suicidal; in fact, on occasion, patients have committed suicide during this initial phase of treatment.

In conclusion, we have reviewed some new concepts involved in the diagnosis of manic-depressive illness and have illustrated one of our research strategies that uses pharmacological agents with specific sites of action to study the causes of manic symptoms. There has been a great deal of progress made in the past decade in the area of affective illness in terms of diagnosis, understanding of the genetic factors, pharmacology, and in the treatment of manic-depressive illness.

II. GENETIC FACTORS IN PSYCHOSES

The demonstration that genetic factors operate in the psychoses was a giant step forward in the long effort to understand mental breakdown. The studies that established the existence of a genetic role in the incidence of schizophrenia are now classics. They offer conclusive proof that biological research has an important place in the mental health field.

Biogenetic research results have also helped to identify some important research projects for the future. The recognition that some persons are genetically predisposed to certain mental disorders suggests new approaches to the problems of prevention and intervention. We can try to identify those who are at risk of mental breakdown by virtue of their biological inheritance. We can work toward the creation of a developmental psychopathology that will clarify the questions of who is vulnerable to psychosis, and what are the environmental factors that influence its onset. Answers to these questions are necessary to the creation of an etiological model of mental disorder, which would help us know how to intervene to prevent or, at the least, to reduce the severity of psychosis.

Daniel X. Freedman, M.D.

The Role of an Emergent Developmental Psychopathology in the Study of Vulnerability to Psychosis

Norman Garmezy, Ph.D.

The role of genetics in the psychoses has passed beyond the stage of hypothesis and now appears to be the most stable reference available to research in schizophrenia and the affective disorders. In a little more than a decade, the genetic etiology in schizophrenia has been affirmed clearly through a series of experimental studies utilizing the methods of twin research and adoption and cross-fostering. These methods have rapidly and rightfully attained the status of classics. The presence of such gene variations provides evidence that there must exist a meaningful biochemistry of the psychosis. This view, long advocated and long elusive, is now so well supported by the evidence that it becomes possible to suggest that the dawn of the 21st century may witness an end to the scourge of madness.

The last observation will be subscribed to by many not as an article of faith but rather one of confidence in the talents of many young and seasoned investigators who are now exploring biochemical processes in the psychoses.

There are those, however, who would assert that mental disorders are myths that exist solely in the mind of the perceiver—that schizophrenia is either a metaphor or a mind-expanding condition, or that it is no more than a label set upon the individual and hence is iatrogenic in its consequences. Last year I asked our first-year clinical psychology students to describe the contents of their undergraduate abnormal psychology courses with regard to a nosology of the psychoses. With depressing uniformity, almost all reported the inculcation of disbelief in classification by their instructors and the repudiation of biological models (camouflaged as *the* "medical" model) accompanied by a neglect in citing recent genetic and biochemical research. Indeed, one instructor in a leading undergraduate college even advocated prison terms for individuals diagnosed as schizophrenic as one means of stopping the insidious labelers of such a hypothetical condition.

The attacks on classification and biology have come from several quarters—from so-called humanistic psychologists and psychiatrists who dispute the validity of diagnosis in psychiatry and question the purposes to which they are put, from sociologists convinced that the explanations of deviance are to be found in that ill-deserved term "labeling theory," from Skinnerian-oriented clinicians who see in the overt behavior of patients a complex of acts acquired solely by social learning mechanisms and thus easily disposed of by various conditioning procedures, and from civil libertarians rightfully concerned with the negative effects of institutionalizing severely disordered individuals as a result of classification. These attacks on classification are part of a cluster of views embracing, among other things, a disparagement of biological processes in mental disorders, a derogation of pharmacological interventions, and a devaluation of the concept of disease or illness in psychopathology.

Such views I hold to be ingoistic and uninformed. They conflict with growing advances in research on genetics and the biochemistry of psychoses. One senses in psychiatry a movement back to medicine and its biological underpinnings. This renas-

cence in biological psychiatry owes an enormous debt to the discovery of phenothiazines and other drugs that affect significantly specific neurotransmitter substances at a biological level while also modifying mood and cognitive states at a behavioral level.

Findings such as these have promoted the beginning efforts to understand biological-psychological interaction in the severe mental disorders. The current vigorous research in this area suggests that the next decade will see the further development of rational drug treatments for schizophrenia and affective disorders, with linkage to etiological models that will seek to relate biological and psychological components in these severe psychotic states.

I am concerned with how well we will be prepared to share in these advances in biological research with comparable discoveries on the behavioral side. This question frames the comments that follow on the need for an emergent developmental psychopathology through the extension of studies of children vulnerable to severe behavior pathology.

The study of risk factors in children is, in its potential significance, equal in importance to the construction of a viable biochemistry of mental disorder. Indeed, there are not only striking parallels in the emergence of these two significant areas in psychopathology but a marked interdependence of one upon the other.

Critics of biological research point to a 300-year history of failure to identify the pathogen for psychotic disorders. Progress is not dated from the first clinical description of the disorder as recorded in the annals of psychiatry, but from the time in which there is an emergence of those sciences fundamental to a meaningful biology of mental disorder. From this perspective, the relevant time period narrows to the final one-tenth of those three centuries. Only since World War II have biochemistry, pharmacology, and the neurosciences become capable of providing the scaffolding for biological psychiatry. The situation is comparable with regard to developmental psychopathology. The opening sentence in a recently published volume begins, "This is a book about a field that hardly exists yet . . ."

Many factors make for such a fragile entry into the world of science. Perhaps the most important is this: Just as the biological psychopathologists had to await the emergence of their basic sciences in order to identify the possible core variables implicated within the psychoses, so too have the developmental psychopathologists—a small band not at all isomorphic with child psychiatrists or child clinical psychologists—had to await the growth of several basic sciences. The most fundamental in content are developmental psychology and developmental biology. In method, a significant basic science is ethology.

Let me begin with method. For those concerned with mental health, adaptation and maladaptation have always been cast in developmental terms. "The childhood shows the man, As morning shows the day" wrote Milton in *Paradise Regained,* and, indeed, it is in childhood that the wellsprings of the mature and immature adult are to be found. Nowhere is the significance of the early critical years more apparent than in the study of the origins of psychopathology. To trace the antecedents of a disordered adulthood, we look to childhood, hoping to find therein the solution to the age-old riddle, "What is it that accounts for that extraordinary range in human adaptation that we daily observe around us?"

Previously we have traced the peculiarly inappropriate accounting that took place in psychiatry. It was an accounting that involved countless inquiries of disordered individuals and countable inquiries of normal ones. All of these people had at least two attributes in common: They were adults and they were asked to look backward into their own lives or those of family members in an attempt to provide insights that would unlock the mystery of the development of deviance or normality in human exchange. The net result of this extraordinary belief in the accuracy of recall was to create an image of personality continuity between childhood and adulthood that, in effect, provided for a psychopathology of childhood that bore all the trademarks of an adult psychiatry. Today, we are more aware of shortcomings of retrospection. Furthermore, biased observations produce

biased data. That bias is nowhere better reflected than in the study of schizophrenia and the family. One need only think back to the fifties when the idea of schizophrenogenic mothers dominated the approach of psychoanalytically oriented clinicians treating schizophrenic patients by dynamic psychotherapeutic procedures. Today, new experimental laboratory paradigms utilize miniaturized cross-fostering techniques in which parents of normal or schizophrenic offspring are studied as communicators and respondents in structured laboratory tasks. These techniques suggest the more likely interpretation of a reactive than an etiological model of the mother's role in the disorder. It is unlikely that psychiatrists would have shown such a steadfast preoccupation with distorted mothers and disturbed children had they turned toward observations of children at risk and of the caretaking behaviors of once diagnosed schizophrenic mothers. Here is the most significant of changes—a fundamental shift in who and what is to be observed and when such observations should be made.

Developmental processes cannot be studied in a vacuum, however. The virtues of the laboratory are well known, but the laboratory and the couch have in common a distance from the naturalistic world. It is important to conduct research into children's adaptations in the richly complex world in which the child moves, thinks, and engages. It is interesting, therefore, to note the growing impact of ethological principles on the study of the behavior of children. Ethograms—those patterns of adaptive behavior that were once the exclusive province of the ethologists—are slowly being integrated into the corpus of developmental psychology. Such systematic and encompassing descriptive accounts of children's behavior in their natural settings may, in time, provide the basis for understanding precursor attributes in potentially vulnerable children. In a recent introduction to a volume on ethological studies of children, Professor Nikolaas Tinbergen, 1972 Nobel Laureate, noted the potential power of ethology for understanding psychopathological development. He said:

> It is . . . surprising how much is being discovered which so far has simply been ignored by the professional psychologists; on the one hand, it is clear that this simple, careful observation of normal children is going to be a very demanding task indeed. But, it will give a wider scope and more purpose to human studies. And, no less important: by gradually building up an ethogram of our species, work such as is represented here will provide the yardstick by which behavioral pathology can be measured.

The words of Sir Peter Medawar could well have been taken as a motto: "It is not informative to study variations of behaviour unless we know beforehand the norm from which such variants depart."

The development of the norms of behavior has long been the province of child psychology, but it was a rather desiccated child psychology with which psychopathologists had to contend through the first half of this century. The necessary catalyst for change and progression arrived in the form of a great figure—Jean Piaget. Piaget's seminal contributions revitalized developmental psychology by providing new theoretical insights into the process of development, overthrowing the notion of the child as a miniaturized adult who is simply awaiting maturity (the "linear growth model"). In its place, Piaget substituted a new view of the child moving through a stated sequence of increasingly complex stages, each requiring unique transformations in behavior that follow upon, but differ from, the preceding stage, and each in turn reflecting increasingly complex patterns of organization and differentiation and higher levels of cognitive and social maturity and competence.

It is the presence or absence of these behaviors at appropriate stages that are most likely to be implicated in analyzing risk potential in children vulnerable to psychopathology. If we see relatively little emphasis as yet on such an orientation in ongoing risk studies, it is because risk researchers are giving initial priority to those variables that have discriminated schizophrenics from nondisordered persons. We must allow developmental psychopathologists the same freedom

to discard non-payoff variables that biological psychopathologists had while they ran through virtually every organ system of schizophrenics before fixing rightfully on the nervous system and brain function.

Piaget has always specifically disavowed an interest in psychopathology. It is interesting, therefore, that in E. J. Anthony's recent volume, *Explorations in Child Psychiatry* (1975), Piaget's foreword addresses the need for an "analytic" approach to the problem of understanding the "mechanisms involved in any particular functional disintegration." He then adds:

> However, since there are those who remain normal in situations where others become variously disturbed, the meaning of the disorder to be remedied can be extremely diverse, and in order to grasp it, it is necessary to immerse oneself in the ensemble (of elements involved) at different developmental stages, the order of which is by no means fortuitous but resembles the orderly stages observed in embryogenesis.

In his conclusion, Piaget comes closest to the ultimate goals of risk research when he expresses his appreciation and awareness of an emergent developmental psychopathology:

> . . . developmental psychologists . . . are looking forward with great expectation to the emergence of developmental psychopathology as a discipline still struggling to organize its own relevant field of knowledge. They are hoping especially that in spite of all the obstacles in the way and the huge amount of creative effort required for the purpose that this science will constitute itself on an interdisciplinary basis as wide as possible and on a common language that helps to unify what is precise and generalizable.

The data that are now emerging speak to developmental issues of transcendent importance. One might consider on the clinical side the work of two psychiatrists whose sophistication is of the highest order, and whose studies have enriched the clinical investigation of children at risk by virtue of psychotic parentage: Dr. E. James Anthony of Washington University and Dr. John Romano of the University of Rochester. Dr. Anthony has provided us with a detailed clinical account, accompanied by richly elaborated case examples, of the consequences of parental psychosis. Drawing on home visits, including living-in with some families, and on individual sessions with family members during periods of ongoing crisis, Anthony has described a triad of family reactions in which outcomes are markedly varied. There are healthy families, demarcated by qualities of competence in their members, which utilize the crisis of parental breakdown for rally and for further growth and differentiation. The potential for recovery in these families is indexed by the same factors that index prognosis in schizophrenia, namely, the premorbid adequacy of its members. There are other families that respond initially with breakdown, and only then rally, while still others are prone to rout and disintegration. Even in the latter families, however, the process can be halted and regenerative efforts can be fostered.

Dr. Romano and his colleagues Dr. Geertsma and Ms. Trieshmann have been attempting to document the personal characteristics of parent and caretaker by using videotaped interviews and a variety of scaling procedures, as well as cataloging such factors as caretaking patterns. The videotaped interviews are magnificent clinical documents of the complexity of family life under the impact of parental psychosis.

A recent report from Dr. Romano and his colleagues states that they have studied 59 families and have reviewed the clinical records and initial inpatient hospital diagnoses of the affected spouses. The attributes of these families in general point to the heightened competence of their members. Again, consistency is reflected in Dr. Romano's observations that ". . . a wide range of parenting attitudes has been observed. Another impression is that regardless of the depth and intensity of the psychoses, appropriate parenting attitudes appear to be sustained."

Clearly, we will need to use a multivariate orientation in the study of developmental psychopathology. Knowledge of parental care-taking practices and measures of func-

tional competency in the child will permit the analysis of variables drawn from a variety of disciplines including genetics, biochemistry (in terms of the role of catecholamine metabolism), and psychology. Risk research is the way station into the unification of these important and diverse disciplines and will provide an enhanced understanding of vulnerable children.

I conclude by paraphrasing. Dr. Seymour Kety, writing on contemporary irrationalisms in the mental health movement, noted recently that "if schizophrenia is a myth, it is a myth with a genetic component." To paraphrase Dr. Kety, I would say that if risk research is a fad, then it is a fad generated by the union of developmental biology and psychology into a new scientific discipline—developmental psychopathology. Given such illustrious parentage, can such offspring be viewed as simply illegitimate or at risk?

242-844 O - 77 - 4

Genetic Studies in Schizophrenia and Depression

George Winokur, M.D.

Maximilian II of Bavaria married Maria of Prussia. They had two children, one of whom was Ludwig II. As King of Bavaria, Ludwig allied himself with Otto von Bismark, freeing Prussia to carry on the Franco-Prussian War of 1870 and planting the seeds for two world wars. Thus, he must be considered a person of some consequence in history.

Ludwig was an interesting fellow. He had a romantic mania for building that led him to construct an ersatz Versailles in Bavaria. At 37 he became withdrawn and extremely paranoid, and at 41, committed suicide by drowning himself. In a vain effort to help, his psychiatrist died with him, going well beyond the call of duty and giving history its first hero of psychiatry. Ludwig's brother, Otto I, should have succeeded him, but this was impossible because Otto had already been declared insane. Is this concentration of mental illness in one family a coincidence or could it be due to genetic factors? Today's data suggest that this kind of circumstance is the result of genetic influence.

There are four reasons for a researcher to engage in genetic studies in psychiatry. First, he can look for specific kinds of transmissions. This turns out to be very elegant mathematically but not so useful for the solution of clinical problems. Second, genetic studies might enable the researcher to predict certain kinds of subsequent clinical circumstances in families and would, therefore, give him a group at high risk. Third, if genetic factors are found to be operating, it proves beyond doubt that there exists a biological factor in a particular mental disease. This would indicate that the biology of the illness should be studied. It does not mean that other etiological factors should not be studied but that a biological factor is of considerable importance. Finally, the main reason to do genetic studies is to attempt to solve the problem of heterogeneity. If researchers are to study neurochemical or other biological factors in particular psychiatric diseases, they must deal with homogeneous diseases. The lack of homogeneous diseases might well hide positive findings. If two diseases are present in any study group, it is quite possible that biological findings will cancel each other out. It is in the area of the separation of homogeneous diseases from the large mass of psychiatric syndromes that genetics has made its major contribution in the last 10 years.

The two major psychoses are schizophrenia and manic-depressive (affective disorder) disease. Twin studies indicate that these psychoses are separate diseases genetically. In a monozygotic twin pair in which one has manic-depressive disease, concordance for manic-depressive disease is very high in the other twin. Schizophrenia, however, is never seen in the other twin. Similarly, if there is one schizophrenic in a monozygotic pair, manic-depressive disease is not seen in the other twin, but schizophrenia is a common occurrence. Manic-depressives have many first-degree relatives with manic-depressive disease and few with schizophrenia. The converse is true for the first-degree relatives of schizophrenics. The conclusion must be that schizophrenia and manic-depressive disease are autonomous illnesses. However, within the broad rubrics of schizophrenias and manic-depressive illness, the data show that there is considerable heterogeneity.

To search for homogeneous entities in manic-depressive illness, we will use a genetic or familial paradigm. Affective disorder

as a broadly defined entity may be separated into a bipolar and a unipolar group. The person belonging to the bipolar group has mania and depression or mania only. The unipolar group contains people who have only depression. Separation of bipolar (manic-depressive disease) from unipolar illness (depressive disease) is one of the success stories in psychiatry. This separation occurred in 1966 when three groups of investigators working independently in Sweden, Switzerland, and the United States showed different familial patterns in the two types of affective disorders. These workers conducted their research independently of each other and used different methodologies.

Bipolar patients have a history of mania, but unipolars, of course, do not. There is more affective illness in the parents and families of bipolar patients than in unipolar patients. There is evidence of X-linkage in bipolar illness. This means that the genetic factor that is involved in bipolar illness is located on the X-chromosome. If an illness is transmitted by a dominant gene on the X-chromosome, it means that there will be more ill women than men. In fact, this has proved to be true in almost all studies. It also means that males cannot transmit the illness to their sons. Over the course of years, this last has turned out not to be true; some bipolar fathers do transmit the illness to their sons. Therefore, the present data indicate that there are different types of transmission within bipolar illness or manic-depressive disease. In one calculation that I performed, I came up with the finding that about 51 percent of manic probands would have their illness transmitted in X-linked fashion and about 49 percent of such probands would have their illness transmitted in a different way. To accomplish such a linkage study, one would take a family where there is manic-depressive illness assorting with a known X-linked marker such as color blindness. Two traits should assort together in a family. This does not mean that the color blindness would be associated with manic-depressive disease. It simply means that within such a family most manic-depressives should be color blind *or* have normal color vision. The linkage is between the two loci on the chromosome, not with the specific trait. There are data that have been collected in both St. Louis and New York from a number of families which support the idea that X-linkage is a significant mode of transmission in manic-depressive illness.

Most affectively ill patients have only depression. It seems reasonable to assume that unipolar illness itself is heterogeneous. We have data which seem to separate out two kinds of unipolar depression, "pure depressive disease" and "depression spectrum disease." Depression spectrum disease is an illness more frequently seen in early onset females. Such females become ill before the age of 40 and also have more depressed women in their families than depressed men. There is a large amount of alcoholism and/or antisocial personality among the male relatives of such patients. If one collects all the illnesses in such families, i.e., depression, alcoholism, and antisocial personality, about 23 percent of the first-degree relatives are ill. This illness is to be contrasted with pure depressive disease which is seen in the prototype of late onset males. Such males become ill after 40. There is little alcoholism in their male relatives. Depression is equally seen in male and female relatives, and the total amount of illness is considerably less than in the depression spectrum disease patient.

It has not been proved whether these two kinds of illnesses exist. One way to prove this is to determine whether linkage would occur between particular genetic markers and either pure depressive disease or depression spectrum disease. We have such a study in progress at present.

There remains the problem of heterogeneity within the large rubric of schizophrenia. There is no question that there is a genetic factor in schizophrenia. The studies of Kety, Rosenthal, and Wender and of Leonard Heston are conclusive. However, a genetic factor may exist only in certain types of schizophrenia. It is necessary to separate out specific types which can be considered in themselves indicative of autonomous diseases.

The first type is organic-symptomatic schizophrenia. Persons suffering from this illness also have a major medical and neu-

rologic illness. This contrasts with idiopathic schizophrenia in which a person has nothing else but a schizophrenic syndrome. The organic-symptomatic schizophrenia patient may have such an illness as epilepsy, Huntington's chorea, or a brain tumor. The family history of schizophrenia in such a person looks very similar to that of the general population. Thus, it is to be separated on a familial basis from the idiopathic group in which the family history shows a higher incidence of schizophrenia than that which might be expected in the general population. Looking at the idiopathic group, we note that it is possible to separate it into three groups according to specific familial pathology. So far we have not found a specific kind of transmission for idiopathic schizophrenia, and I would suggest that this may be due to heterogeneity. I despair of biological findings being clearly demonstrated in schizophrenia until we have settled the problem of obtaining homogeneous subgroups.

Within the idiopathic group, there is a subgroup called "acute." Acute schizophrenics have a high history of affective disorder and a relatively low family history of schizophrenia. There is some question as to whether acute schizophrenics breed true, that is, whether they have family members who also have acute schizophrenia. Our own data indicate that family members have ordinary affective disorders. It is quite possible that acute schizophrenia is either (1) essentially related to affective disorder or (2) is a third psychosis totally different from either schizophrenia or affective disorder. Familial acute schizophrenia is not related to chronic schizophrenia. In evaluating the chronic schizophrenias, the nonparanoid types (hebephrenic, catatonic) show a relatively high family history of schizophrenia and, in fact, show breeding true within the family. Chronic paranoid schizophrenics, on the other hand, show a lesser amount of schizophrenia in a family. They also may breed true within the family.

The data separating chronic paranoid and chronic nonparanoid schizophrenia are essentially culled from the literature. The bulk of the world literature reports this difference in a familial pathology, but the question must be considered open. A study should be formulated which will answer this problem directly. Distinguished studies, such as those by J. A. Book and F. J. Kallmann, indicate that nonparanoid schizophrenics breed true as do paranoid schizophrenics. However, more data are necessary.

For many years we used two ways of evaluating heterogeneity and homogeneity—the clinical picture and the followup. About 10 years ago we started to use a genetic methodology for the same purpose. This has paid off very well, and we certainly have not exhausted the method as yet. There are many years of productive research ahead of us in which the use of a genetic or familial methodology will help to clarify the question of homogeneity.

III. PSYCHOPHARMACOLOGICAL ASPECTS OF PSYCHOSES

The contribution of the psychotropic drugs to improved treatment of psychosis is so well known as to require little discussion. Perhaps less familiar is the shift in recent years from treatment of the acute episode in the psychoses to a pharmacotherapy of maintenance. The pharmacological agents are effective in reducing the occurrence rate of psychotic episodes and in diminishing the extent of psychopathology when an episode does occur. These qualities have made chemotherapy a significant factor in upgrading the long-term as well as the short-term treatment of psychiatric disorders.

In addition to their role as therapeutic agents, drugs have also played an important part in the recent advances in understanding the physiological basis of mental illness. Although their therapeutic use was at first entirely empirical, the effort to understand the mechanisms by which they worked led directly into basic research. There the psychotropic drugs proved to be useful tools. They have provided clues to the normal as well as the abnormal functioning of the brain and so have made a contribution to the increased understanding of brain physiology, one of the major achievements of recent research. There can be little doubt that pharmacological research will continue to be fundamental to the effort to improve both treatment and understanding of serious mental disorder.

Jerome Levine, M.D.

Analysis of the Impact of Phenothiazines and Related Drugs on the Treatment of Schizophrenia

Gerald Klerman, M.D.

There are currently at least two dozen compounds in six or more chemical classes that have been developed in the 20 years since chlorpromazine. The prototypic compound, chlorpromazine, is a representative of the phenothiazine class, the first class introduced by the French in 1952 and Heinz Lehmann in North America in 1954.

Rauwolfia, used in the treatment of hypertension, was a major advance. It is little used today because other drugs are more effective, but were it the only drug, it would be useful. The two other compounds are the benzoquinolizines and the butyrophenones, of which haloperidol is the prototypic compound.

All these drugs, as well as four other classes still in the experimental phase, have three things in common. First, they all reduce psychotic behavior, particularly among schizophrenics, and are also effective against the apathy and withdrawal of acute schizophrenia. Second, they produce a side effect of Parkinsonian illness in the nervous system. Third, all these compounds, particularly the dopamines, influence the central nervous system neurotransmitters.

Let us look at the consequences these drugs have had since their introduction. First, for treatment:

In the NIMH collaborative program, 99 hospitals around the country participated in a double-blind study in which patients with acute schizophrenia were treated with phenothiazines. The results show that 95 percent of the drug-treated patients improved somewhat within 6 weeks. Half of them were symptom free. One-third of the placebo patients improved; we should not forget that, because they represent an important subgroup. One-third of the placebo patients worsened, while only 5 percent of the drug patients worsened. Overall, without a shadow of statistical or clinical doubt, the phenothiazines of three different clinical characteristics brought about improvement. This is true in every country where adequate studies have been carried out.

Next, let us consider the consequences for the health care system. There are relatively few clinical treatments in medicine that have had an impact on the total delivery system.

From 1910 until the turning of the tide in 1955, there was a steady increase—about 10 percent per decade—in the number of patients in mental hospitals. Half of these were diagnosed as schizophrenic. Since 1955 the curve has turned downward. Today, the population of public mental hospitals is only one-third of what it was in 1955, and the numbers are going down at an accelerated rate in almost every State. Whether this trend will continue is doubtful because of the danger from the backlash in many State legislatures in which there is fear that patients are being released indiscriminately.

Extrapolated from the present back to 1955, the data indicate that the rate of inpatient admissions for psychiatric purposes has remained constant at about 800 per 100,000. What has changed within the inpatient segment of the health care system is that the proportion of inpatient care taking place in the public sector has dropped. In 1955, according to Dr. Morton Kramer, NIMH, 80 percent of all inpatient care episodes took place in public, VA, or State hospitals. Today, public hospitals account for less than half of the inpatient care episodes. The shift has been toward psychiatric care in general hos-

pitals. I maintain that one reason for that profound shift is the availability of effective treatments within the mainstream of the medical model.

The other shift is the dramatic and rapid increase in outpatient utilization. After adjustment per 100,000 population, Dr. Kramer's data indicate that, although the inpatient utilization has remained fairly constant, over the past two decades outpatient care has increased at almost astronomical proportions.

The critics of psychiatry may think that we are labeling or producing a myth, but the patients don't believe them. More and more patients are coming in for treatment. A large part of this increase in outpatient utilization occurs, in my opinion, because the public is convinced that we have effective treatment.

There are two other consequences. One is that the availability of the phenothiazines has opened up exciting and dramatic research in the laboratory. It has also opened up clinical psychopharmacology and has set a standard for other clinical research.

There is some bad news. We are paying two prices in the cost/benefit analysis. One price is biological and the other is psychosocial. With long-term maintenance, patients can be maintained in the community, but there is a risk of their developing a prolonged neurologic symptom called dyskinesia. Something like 10 percent of patients treated continuously for 5 years or more are prone to this syndrome. We do not know how to treat it. We do have very good hypotheses about its neurochemical basis based upon the dopamine model.

Next, while our patients are better, they are not well. We can get them out of the hospital, but we cannot completely rehabilitate them. Large numbers of them are living lives of quiet desperation. The closed door has been replaced by the revolving door and the back ward is being replaced by the back alley.

Here, I think NIMH has not done as well in providing the leadership in evaluating community programs as it has in evaluating efficacy or in developing the scientific basis for treatment. In legislatures and in influential journals there is criticism that the community health programs are dumping schizophrenic patients into the community where they are mistreated or are unable to take care of themselves.

We do not have data to refute this. I cannot tell you how many schizophrenics in a given community, such as the one in which I serve as Director of a Mental Health Center, are functioning at what level of competence. The newspapers pick up the horror stories of the welfare neighborhoods of New York or San Jose. Whether they represent the tip of the iceberg is hard to say at this time; we do not have hard data. I think that they are atypical.

My experience is that most patients in properly controlled community programs, with day programs and visiting nurses, do very well. There are no back alleys in Massachusetts. There are no more than 12 patients under any one roof. There are no welfare hotels. We do not yet have hard evidence on the psychosocial consequences of community treatment that parallels the elegant evidence of the biochemical research. I hope we will take the opportunity to use the scientific knowledge of research design and epidemiology to study the psychosocial consequences of community treatment and to turn back the backlash.

The Impact of Lithium on the Treatment of Manic-Depressive Disorders

Samuel Gershon, M.D.

The modern era of psychopharmacology was inaugurated by a specific drug therapy for manic-depressive illnesses. Joseph Cade's report in 1949 claimed efficacy of this treatment of mania. That report is the dateline, the year One for psychopharmacology as a major discipline in psychiatry.

Before the availability of specific chemotherapeutic agents, only electroshock and nonspecific therapy were available for patients with depression, mania, or behavioral disturbances. I stress this to demonstrate that in a relatively short period of time we have gone from a completely haphazard, random, unknowing approach to treatment to what we have to offer today.

This pattern of nonspecific treatment no longer exists: We now have effective chemical treatments available. And, although we have not obtained airtight postulations of specific chemotherapy, we have some ways that might permit us to approach this goal.

Lithium may serve as one example of what has happened. This agent, historically and pharmacologically, has a unique place in both treatment and research of affective disorders. The therapeutic use of lithium was first reported in 1949 in the *Medical Journal of Australia*. It was at least 10 years after that report before any significant notice was paid to this discovery, especially in the United States.

Let's look at the effect of lithium on the treatment of manic-depressive disorder. This illness has a wide range of manifestation. When a patient is hospitalized or treated as an outpatient because of an episode of this disorder, he appears in the statistical data on manic-depressive disease. But the statistics are silent on the impact of the illness in its lesser forms. Some of the people at the lower end of the pathology do not appear in statistics, as either patients hospitalized or attending outpatient facilities. Yet the milder forms of this illness, whether in the manic or the depressive phase, also cause significant problems for the individual and for his family. The disease is also cyclical. The patient is ill, he may be well, then ill again. The frequency of episodes can vary.

Now let us consider what happened when lithium was introduced. Cade reported giving lithium to 10 manic patients and the observations that he made on those 10 patients have not been significantly challenged in the subsequent 25 years of research.

In analyzing the data accumulated since his observations, and generalizing somewhat, we can say that lithium is now established as an effective treatment for the manic phase of this illness. Second, and even more important, is the established fact that lithium can either prevent recurrences or diminish frequency or intensity of episodes. It is this ability to prevent repeated episodes that is most important for the individual and his family. Third, data accumulated over the years, and more recently established by some NIMH authorities, indicate that lithium has some prophylactic effect in controlling concurrent episodes of depression in affective illness. It acts to control depression in the unipolar as well as in the bipolar form of the illness.

The fourth point is not yet firmly established, but there is some suggestion that lithium also may be of some efficacy in treating a current manifest depressive illness. If this is true (and it has certainly not been established absolutely), it would be of great importance for the biological research ap-

proaches necessary to explore both the mode of action of this agent and the biology of the disorder.

These clinical findings, in addition to their tremendous importance for a patient and the patient's care in the family, have dramatic import for the investigator as well. They give him a benchmark and the assurance that these data can be explored meaningfully in a laboratory.

Lithium is also unique in other respects. It does not have significant undesirable behavioral effects on the patient. Most other agents do have additional, negative effects. Thus, lithium might approach the ideal of a specific therapy with minimal side effects.

Finally, there is significant evidence to suggest that lithium affects both aspects of manic-depressive disorder. It does not seem to be controlling a symptomatic profile of a phase but appears to be attacking the disease. This is open to question, but it is a possibility that I would like to suggest. There are other agents available for the treatment of affective disorder. The tricyclic compounds and the monoamine oxidase inhibitors are useful in treating the depressive phase.

These agents can control the current manifest depressive phase of a bipolar illness but, as seen in the NIMH study, they will activate the manic phase. Therefore these agents cannot be used successfully in the long-term treatment of bipolar patients with recurrent depression.

There are problems with all of these treatments; even with lithium there are some, but in the behavioral area they are minimal. In treating a current manifest depression, our major difficulty is the speed of onset. Effective drugs take more than several days to work. This is significant in treating a severely depressed patient in the hospital but even more so when he must be treated as an outpatient.

Also these agents have certain side effects. The anticholinergic side effects include some minor problems such as dry mouth and blurred vision. But in the elderly they are more serious: confusion, disorientation, and so on. Therefore, one of the goals of research must be to find agents that are faster in onset and that can be used without side effects and for a broader spectrum of the population.

A number of areas in chemotherapy await further development. The data indicate that the indications for treatment may be broadened. Prevention, for example, is a standard topic of conversation and the standard medical treatment of disease. While prevention has been known in psychiatry, it is not yet considered an important possibility. The work with lithium and recurrent disorders suggests that some psychoactive drugs can be effective in prevention as well as treatment of psychotic episodes.

Work with the antidepressants in recurrent unipolar depressive episodes and in depressive illnesses by Dr. Klerman and researchers at Johns Hopkins has shown that these agents also can diminish the recurrence of depressive episodes. This is an important area that should be explored and utilized at the delivery end.

There is also a group of depressive reactions that has been in large measure ignored. Post-traumatic depressions have rarely been treated. There are many individuals who develop postsurgical depressive reactions even to the point of suicide, yet they are rarely treated with pharmatherapeutic agents.

Finally, there is depression in the elderly. It has been talked about and written about for years, but it has not yet become a target for an established chemotherapeutic approach, nor have we data defining it clearly. Depression in the elderly is not only the depression that is seen by the psychiatrist and recognized by him. These people are mainly referred to as senile. They are dumped. They have the features of organic deterioration, but many of these are depressive analogs and do respond to chemotherapeutic intervention.

Pharmacological Research and the Psychoses: An Overview

Morris A. Lipton, M.D., Ph.D.

The psychopharmacologist is concerned primarily with two kinds of questions about the relationship between the chemical neurotransmitters on the brain and mental illness. First, he wants to know whether there are quantitative changes, that is, whether there is too much or too little of the transmitter. Second, he asks whether there are qualitative changes through which a transmitter is modified in some fashion so that it becomes a false transmitter and thereby jams the works. Much of the work in psychopharmacological research comes from those questions.

The very fruitful interaction between psychopharmacology and the basic sciences goes back to the discovery of the psychotropic drugs. Almost every psychotropic drug was empirically derived; there was no theory for lithium or the tricyclines. The need to understand their mechanisms sent us back to the basic sciences for answers, for there is no other way to understand these mechanisms.

This interaction will certainly continue. It has already resulted in some highly relevant information, but there is still a long way to go. In genetics, for example, there is a desperate need for real genetic markers. As a biochemist, I would like to think that we will derive those genetic markers from biochemistry, perhaps in the form of enzymes. But I must point out that Victor McKusick's book on Mendelian inheritance, the simplest form of inheritance, lists some 1,800 genetic diseases of which only 150 have biochemical origins. That is only 7 percent. I recently learned that the oldest of all known Mendelian diseases, Mendel's wrinkled pea, still has no known biochemical explanation. We still don't understand the factors that cause that pea to be wrinkled.

There is much to learn, too, concerning levels of treatment. As most of us recognize, the infectious illnesses and the nutritional illnesses are really the only ones we can cure. The rest we treat. Hypertension, arthritis, and diabetes we treat with more or less success. And we are quite successful in the treatment of the affective psychoses. I would venture to guess that we are about as good in that area as the internist is in the treatment of diabetes with insulin. Recovery rates are high and there is relatively little disability, although flareups now and then do require treatment.

The record is not so good in schizophrenia. There is a high morbidity rate for schizophrenia, and the cost of this illness today is $17 billion annually. That is about two million cases at about $8,000 a case. We need to improve in this area. How can treatment of schizophrenia be improved? One way is to develop better drugs, drugs that act more rapidly, more specifically, and with fewer undesirable side effects. I think such drugs can be derived.

Perhaps another approach is to recognize that until now we have attempted to deal with one transmitter at a time. We have looked for something that will affect dopamine or norepinephrine or serotonin. The odds are that the brain doesn't operate that way. It is more likely that the transmitter systems interact. We may be able to come up with some rational combinations of drugs based not on symptoms, but on how the brain acts. There is a recent report from Sweden, for example, to the effect that the phenothiazines, plus a compound which may be a

gamma aminobutyric acid precursor, may permit lower doses of phenothiazines.

Beyond that, we are in the area of the environment. Unfortunately, the environment so far as we can tell is not specific for the psychoses. We certainly cannot define an environment that will prevent schizophrenia. We have difficulty in defining the environment that will prevent relapses in this disease.

Thus, there is still much to do in this field. Progress has been made. We have eliminated a good deal of untenable theory and are better able to define precisely the ever more complex questions that need answering.

I do not look for miracles, but I do expect some significant advances in the treatment of schizophrenia in the next decade.

IV. PSYCHOPATHOLOGY OF PSYCHOSES

Psychosis, like other human problems, looks increasingly complex as we study it. The social scientist is most aware of the psychodynamic forces that lie behind deviant thinking and behavior; the biological scientist thinks of the biogenetic factors. In research, the focus has shifted over time from an almost wholly psychodynamic approach to the more recent concentration on the biological substrate underlying mental disorder.

While such variations in emphasis are perhaps inevitable in a developing field, it is important to avoid polarization. It will require a multidisciplinary effort by many people, working cooperatively and responsively with one another, to provide the kind of answers needed for understanding in this field. Research will need to take into account the powerful and still unknown effect of culture on mental illness as well as neurobiological influences. It will take time, but the wide-ranging research of the past 25 years offers both a model and the promise of success.

Martin M. Katz, Ph.D.

Psychopathological Factors in Psychoses

Martin M. Katz, Ph.D.

Psychopathology is the scientific study of mental disorders from the psychological and sociocultural points of view. These scientific perspectives are central to the problem of how we define and identify psychosis.

We are very impressed with the recent important advances in the biological understanding of the mechanisms of psychosis. We are, however, equally concerned that new shifts in emphasis in the research field do not lead to increased polarization in our concepts of psychosis. There was a time, not too long ago, when all our thinking and attempts at research on the etiology of disorders were dominated by psychoanalytic theory. We have had to relearn since then that psychosis is a condition of the "whole organism." It is neither biologic nor psychologic. It would be unfortunate if this new evidence, if these important new theories of biological mechanisms, were to result in a new kind of polarization and lead to a neglect of research on the psychological and sociocultural influences in the causation and shaping of psychosis.

Certain data now appearing emphasize the importance of a sense of balance in this continuing controversy. Most of us are familiar with the World Health Organization study of schizophrenia in nine countries. NIMH has supported that program for many years. The initial objective was to determine through the use of standard methods whether schizophrenic patients could be identified in nine different cultures, and then to develop procedures for estimating the prevalence of this disease in the world. Both western and nonwestern countries were represented. Patients were screened and diagnosed very rigorously.

The methods of interviewing and diagnosing these patients were standard. As expected, schizophrenics could be identified in the nine countries, and a "core" group was found that was similar in the major characteristics of the disorder across all these national situations. That particular finding was not in itself radically new. It did not and will not change the direction of thinking on research in this field. Many clinicians and theorists in the field of psychopathology would have predicted such a result.

What is very unusual is some new, unpublished data pointing to the fact that 5 years later these same patients appear to be following a wide range of pathways. The schizophrenic patients from the western countries follow a course that most western clinicians expected and that the early Bleuler and Kraepelin writings would have predicted. Some residual symptoms remained, many major symptoms receded; but, regardless of the current symptom picture, the schizophrenic "quality" remained. It is in the nonwestern countries that many patients who were identified as clearly schizophrenic at the beginning of the project no longer look very schizophrenic 5 years later.

Now, if this had occurred in the western clinical atmosphere where there is intensive concern with improvements in treatment, we might attribute these differences in outcome to new treatments. But we are talking now about the nonwestern, developing countries, and it is unlikely that the high-quality, high-powered treatment that we see in our own hospitals is being used in these situations. It seems to me that this phenomenon points up the power of culture, of different cultural situations, of psychosocial factors; certainly it indicates the effect of something other

than the demands put on the human system by biological forces.

It reminds us again that as yet there are no biological indices of psychosis. There are no laboratory tests. Psychosis is identified through deviant manifestations in behavior, in thinking, in perception, and in the emotions.

The central question still remains: Are we seeing in psychosis the outcome of a breakdown in the psychological and physiological functioning of the organism, as one describes an "affliction" or disease? Or does the whole pattern of normal or deviant behavior represent an organized effort, integrated at a deeper level of consciousness, to adapt to what is an intolerable psychological experience?

Social scientists are likely to think in the latter framework, to see the adaptation and the deviant behavior in psychosis as being purposeful, aimed at effecting some major intrapersonal and interpersonal changes in the patient's life. We are learning to see and to measure different classes of behavior in psychosis, the behavior which evidences breakdown, and that which appears to reflect the adaptational effort. Learning how to separate them will eventually contribute to unraveling the meaning of this most complex human condition.

But there is, as we all know, a long way to go in this sphere. Why should we expect to unravel the meaning of disorder or the forces that create deviant behavior more rapidly than we have been able to understand the basis for and the varieties of "normal" behavior? What we have been doing in the field of mental disorder over the past 30 years is bringing the same wide-ranging investigational approaches to its study that have already been applied to the study of biology and behavior generally.

The prime example of an attempt to integrate a multidisciplinary, multiscientific attack is the current program at NIMH on the psychobiology of depression. Here we hope to turn the new technology and theories of biology, psychology, and the sociocultural sciences onto this condition and to begin to examine several human systems simultaneously. We are beginning to fashion the necessary links among wholly different ways of thinking and working. We are obviously better prepared in some areas of science than in others to do this, but we look forward to these new integrative developments with enthusiasm.

An Overview of the Psychopathology of Psychoses: Past, Present, and Future of the Biometric Approach

Joseph Zubin, Ph.D.

Before World War II, psychopathology was largely in the hands of phenomenologists who described the internal and external behavior of patients as they observed and perceived it. Kraepelin, Jaspers, Freud, and their followers enriched the heritage of phenomenological observations that came down through the ages from the days of the Ayure Veda, 34 centuries ago. But since no successful therapeutic interventions emerged from these observations, they became static and largely academic, while the patients stagnated in custodial care.

After World War II, with the spread of psychiatry and clinical psychology beyond hospitals and into clinics and private practice offices, a more dynamic approach to observation, including active intervention, took place. Physical therapies and, later, drug therapies and behavior modification developed, and the plethora of options for treatment demanded selection and evaluation. Psychologists and psychiatrists were caught short by this demand. There were no tools available for reliably diagnosing and evaluating the new therapies. There was a need for the development of an objective, systematic approach to descriptive psychopathology to replace the intuitive, freewheeling observational approach. To meet this need, the biometric approach was born.

The available psychological measures ranging from intelligence, personality, projective and sorting tests to expressive techniques like handwriting or drawing were unsatisfactory. Their evaluation, except for intelligence tests—not very useful in the psychoses—depended on the clinical interview, and the latter proved under close scrutiny to be highly idiosyncratic, unreliable, and invalid. We decided in the 1950's to do something about this and, aiming our psychometric techniques on the interview itself, transformed it from a blunderbuss to a sharp shooting rifle aimed at specific behavioral characteristics. The vast universe of observation of the mentally ill during the last 34 centuries has been codified and systematized and analyzed into its underlying components. The resulting armamentarium of systematic structured interviews and rating scales has proliferated into quite an industry; and, sometimes, like the sorcerer's apprentice, I wish I could stop this proliferation and return to the careful clinical observations of yesteryear.

There is danger now of stagnating again, this time on the computer rather than on the back ward. However, these techniques are so much more reliable and valid than the freewheeling clinical interview that, despite dangers of stagnation, they earn their keep. They have been most useful in evaluating the newly developing drug interventions. But not all therapeutic interventions are benefiting from these new tools. Apparently there exist, in the field of testing and of therapy, grandfather clauses similar to those that exist in the field of licensing practitioners. Psychoanalysis and psychotherapy, which came in before the biometric wave, remain immune to evaluation, even as the Rorschach technique still survives despite the critical evaluation of its efficacy. Only the new projective techniques like the Szondi came a cropper under critical evaluation. But the new drug therapies are fortunately undergoing critical evaluation by means of the biometric tools, and the good are being separated from the poor

techniques. It is to be hoped that the newly developing psychological therapies will also not be permitted to thrive unchallenged. This applies especially to the group and confrontation marathons which, to quote Donald T. Campbell and C. Alan Boneau, range from those "... providing comforting solace for fellow sufferers to those proffering the cleansing cruelty of honest criticism from groups of peers one doesn't have to live with." The first step in this direction has already been taken.

The virtue of biometric techniques is that they are comparable from patient to patient and even within the same patient from one interview to another; they are comparable across interviewers if these interviewers have received adequate training; and they meet criteria of reliability and validity to satisfy even the most critical psychometrician. Biometric techniques are not perfect, however. They lack accepted definitions of terms, so that, for example, anxiety does not always mean the same thing cross-culturally. They also cannot provide safeguards against broadening or constricting the inclusiveness of diagnostic categories. For the first difficulty of cross-cultural (and sometimes intracultural) definition of terms, we still have no ready solution except through training with the help of videotapes of interviews depicting the various crucial behaviors. For getting better agreement on diagnosis, we do have a solution. J. P. Feighner's group has proposed an operational definition of schizophrenia and the other mental disorders for the *Diagnostic and Statistical Manual* of the American Psychiatric Association (DSM III). The proposed system provides explicit criteria which are in the form of sets of items, a specified number of which must be present before a diagnosis can be made. To deal with subjects or patients who do not meet the required criteria for any diagnosis, a category of "undiagnosed psychiatric disorder" or "no psychiatric disorder" is provided. Utilizing these research diagnostic criteria, R. L. Spitzer and J. Endicott have shown that the reliabilities of diagnostic decisions rise considerably.

Other advances consist of developing an anatomy of psychopathology by dissecting out dimensions of psychopathology through factor analysis methods and separating such important factors as anxiety from depression which formerly were compressed into the same component. These dimensions help in clustering like-minded patients into homogeneous subgroups on the basis of similarity in profile or in response to treatment. This typological approach aims at bridging the gap between the Kraepelinian approach of disease categories and the Bleulerian approach to syndromes or Meyerian reaction patterns.

Another innovation in descriptive psychopathology is the utilization of the computer in arriving at a diagnosis. By simulating the clinical decision process, we can obtain independently of the clinician a reliable diagnosis which seems to agree as well with clinical diagnoses as one clinician agrees with another.

These new interviewing methods have demonstrated their value in two major studies —the United States-United Kingdom Diagnostic Project and the WHO Pilot Study in Schizophrenia (1973). The U.S.-U.K. project was initiated to determine why the national statistics for schizophrenia and affective disorders show such widely discrepant ratios in the two countries, with the U.S. showing a predilection for schizophrenia and the U.K. for affective disorders. (The ratio of schizophrenia/affective disorders is 2:1 in the U.S. and only 0.5:1 in the U.K.) When our systematic structured interviews were applied by the U.S.-U.K. project staff to samples of admissions to the two countries, and a systematic glossary and diagnostic criteria were adhered to, the differences between the two countries turned out to be not in the patients but in the psychiatrists. Similarly, the ratio of first admissions for functional psychoses to chronic organic brain syndromes was found to be 10:1 in the U.S. and only 0.5:1 in the U.K. But here, too, these differences disappeared when our systematic approach to diagnosis was applied. The WHO Pilot Study in Schizophrenia found specific syndromes of schizophrenia ubiquitously in the nine contrasting developing and advanced cultures that this study investigated from Washington to Ibadan.

Another innovative approach in diagnosis is due to the behaviorally oriented therapists who, finding classic diagnosis of no help in their work, eschewed it in favor of a behavioral analysis. F. H. Kanfer and G. Saslow have pioneered in this area and have focused on those aspects of the individual and his environment that are of immediate relevance to therapy. Behavioral analysis is functional, not topographical, stressing not the presence of a symptomatic behavior but the contingencies under which it arises and those which maintain it. Observation of these contingencies is the focus of the method, and intervention based on learning theory is the basis for treatment. The general outline of behavioral analysis is already available, and, although it has not yet become a generally accepted method, it seems promising for at least certain disorders. Whether it will suffer from the same limitations that delimit behavior therapy itself remains to be determined.

Description, however, is not enough. We must look deeper if we are to find the causes of mental disorder or to intervene successfully in the rehabilitation or even prevention of mental disorders. Ever since early man trephined skulls to eject evil demons, attempts have been made to divine the sources of mental illness. These attempts can now be formulated as scientific models on the basis of which hypotheses are projected and experimental work done to test their tenability. The current models can be classified as either biological or ecological, the former dealing with genetics, internal environment, and neurophysiological approaches, the latter with developmental, learning, and environmental approaches.

Each of these approaches has contributed to the deeper understanding of, and better intervention into, mental disorders, but none has captured the entire field singlehanded. Interaction among them is fruitful. Perhaps the most salutary view is to regard the casualties of mental disorder as vulnerable individuals who, when given more stressful life experiences than their thresholds permit, develop an episode of illness. Eventually, we hope to discover the components of this vulnerability, but at present it may be best to regard vulnerability as the focus, even while searching for its causes. How to measure vulnerability is the task the biometrician is now facing.

Unfortunately we do not yet have ways of measuring vulnerability nor ways of measuring the triggering life events that elicit an episode. We can, however, develop models for conceptualizing the interaction between such events when they become available.

Measures of life-event stressors such as those which F. H. Holmes and R. H. Rahe have developed may prove to play a role in the environmental triggering of an episode similar to the role played by degree of consanguinity in the genetic elicitation of an episode.

Individuals with low vulnerability require a tremendously stressful life event to catapult them into an episode, while those with high vulnerability require but a mild stressor. Once the stress drops again below the threshold, however, the episode ends and the individual returns to his premorbid status. He returns to his place in society and is regarded as recovered. However, if his premorbid level was poor, it is often difficult to tell whether the episode is over; if he could not cope with life exigencies before the episode developed, he will still seem incapable of coping when the episode ends. This may be the reason why it is generally believed that good premorbids tend to recover while poor premorbids do not. In actuality, both recover from the episode, but the recovery cannot be seen in the poor premorbid. In addition, the episode experience may further reduce the coping ability of the poor premorbid.

It is so well accepted that the episode in the affective disorders is time-limited; it needs no further discussion. Whether it also holds true of the schizophrenias is not so well accepted, but the following sets of data seem to make it at least tenable: the disappearance of the catastrophic deteriorating schizophrenias, the shortening of hospital stay to briefer and briefer durations, the return of 50 percent of schizophrenics to self-support in the community, the rehabilitation of the other 40 percent who relapse even though 10 percent remain chronically ill. Even these 10 percent may not really be

having enduring episodes, since at least some of them may be victims of our system of care and social injustice. My own tentative conclusion is that the mentally ill may not be diseased all the time—they may be vulnerable continuously, but not diseased or disordered continuously.

The biometric problem is to devise methods for gauging vulnerability, detecting the beginning and end of episodes, measuring life-event stressors, measuring coping ability before and after episodes, and measuring competence. Thus, while we rejoice in the success that biometric methods have already attained, we still have a long task ahead.

We need to distinguish between indices marking the beginning and ending of episodes, the state-related markers, from those which mark the degree of vulnerability, trait-related markers. Investigations of the presence of these markers in relatives and discordant identical twins can help find the trait-related markers. The state-related markers can be discovered by examining their presence during the episode and their subsequent disappearance when the episode ends.

As for the future of the biometric approach to the psychopathology of the psychoses, several trends are developing. The development in descriptive psychiatry has reached the point where the reliability of the interview results is reasonably high and the operational nature of the diagnosis reasonably established. Still to be demonstrated is the validity of the diagnostic categories. Some predictive validity has been established through followup studies which tend to show that those diagnosed as depressives tend to stay in the hospital for shorter periods than those diagnosed as schizophrenics. Concurrent validity is being sought in certain neurophysiological responses. For example, the critical duration for sensory integration is shorter in schizophrenics suffering with thought disorder than in depressives and normal controls. Manic patients tend to have higher auditory thresholds and, in addition, show a facilitation effect in their reaction times. These two examples demonstrate that techniques can be found in which the performance of mental patients is "superior" to that of normals; in this way, we eliminate the possibility that the observed difference was due to poor motivation on the part of the patients. S. Sutton reviews several other techniques in which significant differences are observed between patients and normals. If we are fortunate enough to develop such markers of vulnerability, and the entire gamut of models from the biological to the ecological are beginning to develop such markers, we could institute preventive methods geared to improving poor premorbid personalities while treating the good premorbids with "benign neglect," since their episodes are self-curing and they usually return to their good premorbid coping ability and competence soon after the end of their episode.

With regard to the reduction of vulnerability, if it is indeed possible, the paths to pursue are probably the following: We can reduce vulnerability temporarily by means of suitable pharmacological agents. Whether we can ever redress permanently the biochemical and personality imbalance which may lurk behind vulnerability is still a moot question. We can also reduce vulnerability by desensitizing the person to the threatening nature of life-event stressors either through behavior modification or psychotherapy. Perhaps an integration of the biochemical and psychological approaches is called for.

To summarize, the psychoses are gradually yielding to the biological and ecological assaults. Both approaches are needed if we are to make any headway. The day of blind forces, whether biological or environmental, driving man to his fate is gone. In our discussion of the etiological models it may have appeared that we consider the individual as either a pawn of ecological pressures or as a slave working out his hereditary fate. This is hardly a true picture of man. For a better definition of vulnerability in which man's personal freedom and integrity are maintained, we must follow J. R. Audy, and look to a concept of health as the maintenance of a dynamic equilibrium against insults continually emanating from the chemical, physical, infectious, psychological, and social environment. When this equilibrium is disturbed beyond its capacity to reinstate its own homeostasis, a disorder ensues. It is

man's personal freedom and integrity which are threatened by mental disorder, and it is the reduction of this threat that commands our efforts in the future.

What are the forces that today threaten man's ability to cope with his environment and how are they being dealt with? It is debatable whether psychopathology is actually on the increase, but it is quite clear that society's capacity to deal with psychopathology seems to be faltering. The institutions developed in our culture to deal with anxiety, depression, and other psychopathological influences have broken down. The church, the family, marriage, and social networks do not function with the effectiveness they once had. For the most part, they seem to serve goals and functions no longer desired. Thus, most of our churches are primarily salvation oriented, family and marriage largely procreation oriented, and employment primarily age limited. Our economic system is primarily profit oriented, our health systems primarily disease oriented, and our research programs primarily discipline oriented. The treatment systems and research programs we have developed are primarily institution or profession oriented rather than problem oriented. The established order is too much with us, preventing the viewing of problems in their totality. The current orientation in economics, health, treatment, and research is ill equipped to deal with the problems presented by the health needs of our population. If we are to meet these needs, we can no longer let profit, disease, and single perspectives rule. We must not limit our efforts to but one scientific model—the disease model—even if it has been so phenomenally successful in the past, nor be merely discipline centered in research. Only by becoming problem centered and by permitting coalitions of disciplines to work toward solution of problems can we hope for progress. Interdisciplinary coalitions are the key to future success in research psychopathology.

Keys to Understanding and Treating Functional Psychoses

John S. Strauss, M.D.

The conceptualization of the psychoses was revolutionized when Kraepelin differentiated these disorders on the basis of their outcome. Major advances in understanding followed from his work. But along with these advances, a dualism that has been characteristic of much scientific progress also arose. One school of thought focused on careful description and diagnostic characteristics of large numbers of patients; the other, working intensively with smaller numbers, focused on attempting to uncover the psychodynamic processes underlying the striking symptoms, signs, and course of these disorders.

The first school generally followed the Kraepelinian tradition, stating that one of the main characteristics of schizophrenia was its deteriorating course in contrast to the remittant course of manic-depressive disorder, the other major functional psychosis. The descriptive school also believed that the functional psychoses were relatively stereotyped diseases or groups of related diseases with specific pathological processes and specific, probably organic, causes. Treatment was aimed primarily at symptom alleviation or at curing the supposed underlying organic defect.

The second school, championed especially by Adolph Meyer, had a particularly powerful impact where psychoanalysis and psychodynamic approaches had become predominant forces in psychiatry. Meyer, Harry Stack Sullivan, and their followers emphasized the variability of outcome in schizophrenia and the specific historical development of psychological processes within the individual. These processes included both the developing adaptive behaviors and the maladaptive psychological patterns which schizophrenic behaviors were believed to reflect. Instead of viewing these disorders as relatively immutable disease processes, these psychiatrists saw psychotic symptoms as having predominantly psychosocial origins requiring predominantly psychosocial treatment. One shortcoming of this approach has been that therapists with this orientation are prone to overlook crucial symptoms in their evaluation of patients. In European psychiatry, the Kraepelinian school dominated. In American psychiatry, followers of Meyer's thinking were generally predominant.

These two schools produced many significant developments in descriptive, biological, and psychosocial concepts of the psychoses. However, about 15 years ago serious disillusionment appeared among followers of both groups. In the United States, the hegemony of psychodynamic schools began to wane as it became clear that the results originally promised were often not realized and that the psychodynamic concepts used and the explanations given were not concrete enough to be scientifically proved or sometimes even tested. At the same time, young psychiatrists in Europe began to demand more psychodynamic orientation toward dealing with the psychoses, complaining of the limitations and dehumanizing aspects of the descriptive-organic models.

Recently, a development has occurred that may save both the psychodynamic and the descriptive-organic groups from simply shifting to the orientation of the other. Methodological progress in clinical data collection and analysis has revealed that understanding what happens to a patient's symptoms and functioning after the onset of psychosis, and the determinants of such outcome, may lead

naturally and necessarily to combining the findings and orientations of both schools.

The first of these methodological advances has been the development of semistructured clinical interviews for collecting information from patients and informants on symptoms, psychiatric history, characteristics of premorbid function, and outcome. These interviews utilize written forms that specify the kind of questions that must be asked of patients and other informants in order to maximize the reliability of the information obtained. At the same time, these schedules also permit the clinician-interviewer to explore freely with the informant the exact characteristics and circumstances related to each of the questions asked. This apparently humble development in collecting clinical psychiatric information has helped to overcome a major hindrance to progress in understanding, preventing, and treating the psychoses. It allows the interviewer to use his clinical skills while establishing a structure that permits comparison of findings from many patients and many investigative groups. It also helps to prevent the bias that creeps in when an investigator with a theory reports on a large number of patients relying mostly on his recall of their characteristics or when a therapist is invested in his treatment and unwittingly convinces himself of its effectiveness whether it works or not.

The second major methodological advance is the increasing sophistication in computer analysis of the detailed data from semistructured interviews. Techniques such as multiple regression and discriminant function analysis aid in understanding which combination of variables best predicts outcome and what characteristics define a specific group of patients. It is now possible to determine far more accurately than in Kraepelin's time the relative contributions and relationships of the many variables affecting a patient's course and outcome. Exploratory techniques, such as cluster analysis, multidimensional scaling, and path analysis, make it possible to investigate objectively what patient characteristics occur together, how stereotyped or variable these groupings are, and to explore the complex causal relationships that appear to characterize the functional psychoses.

The third methodological advance has been the increasing use of careful procedures for subject sampling and comparison. For example, since it is now understood that the group of patients under investigation must be truly representative of the larger group about whom conclusions are to be reached, the errors of the past in seeing chronically hospitalized back ward patients as representative of all individuals with schizophrenic symptoms can be avoided.

These methods are beginning to provide the information so emphasized by the Kraepelinian orientation: careful attention to description of the patient, diagnosis, and outcome. But that very focus has produced research results showing not the stereotypes of outcome, but the complex nature of outcomes and their determinants. In this unexpected way, the newer methodologies have combined both the Kraepelinian focus on careful description and the Meyerian focus on intensive understanding of the complex contributors to psychotic behavior and its outcomes.

Specifically, these advances in method have significantly contributed to the following discoveries:

1. It has been determined by different investigators that schizophrenic symptoms do not herald a disorder with a consistently poor outcome, but that, in fact, the outcome of patients with these symptoms is highly variable, with approximately one-third or more of such patients recovering completely or almost completely, and less than one-third developing a deteriorating course. This finding demonstrates the magnitude of individual variation in the outcome of schizophrenia and suggests that a simple disease model is inadequate to explain this disorder.
2. Many studies have demonstrated that both outcome and its predictors are complex phenomena. Outcome function appears to consist of at least three major processes, each somewhat independent of the others. These processes are the ability to relate socially, the ability to function in an occupational capacity, and

the level of symptomatology. None of these processes can be assessed accurately and entirely by knowing the others, although they have important interrelationships. The demonstration by controlled studies of the complex nature of outcome supports those anecdotal reports that describe patients with no apparent symptoms who lead essentially vegetative existences, shut up in a family house, boarding house, or psychiatric hospital, while other patients with severe delusions or hallucinations, for example, may have active and effective careers and carry on meaningful social relationships. Unfortunately, many mental health professionals have never seen this kind of situation, since such people rarely come for treatment.

The independence of these various outcome functions is further supported by evidence that treatments may be rather specific for one area of disability and rather ineffectual in another. For example, psychotropic medications are effective for symptom reduction, but may not be helpful for, or may even impede, social and occupational adjustment.

3. Recent findings also demonstrate the importance of both biological and psychosocial factors in predicting the occurrence of the psychoses, their course, and outcome. In the biological realm, there is evidence that genetic factors are important contributors to prediction of the course and outcome of psychoses. Psychosocial factors have also been demonstrated to be important in this regard. One of the most powerful predictors of outcome characteristics in the psychoses is the individual's level of social relationships prior to the onset of symptomatology. The importance of social relationships is, of course, at the very center of most psychosocial and psychodynamic concepts.
4. The findings about the importance of genetic and premorbid levels of social relationships in predicting outcome, and about outcome being composed of at least three factors, provide keys to resolving the Kraepelinian-Meyerian split of whether to focus on a pathological process or on coping and adaptation patterns. The answer appears to be that it is essential to recognize both pathological and adaptational aspects of the psychoses.
5. In treatment, both psychosocial and biological factors have also been demonstrated as crucial. Psychosocially, it has been shown that earlier treatment methods, especially long-term institutionalization in poorly staffed facilities isolated from the community and the family, contributed significantly to the deteriorating picture described for schizophrenics. This crucial finding has led to community treatment orientations and involvement of families in treatment procedures and planning, and appears to have greatly reduced the deterioration that was originally considered to be the usual outcome of schizophrenia. In the biological realm, psychotropic medications have played a major role in controlling symptoms and allowing patients to remain in the community.

It appears, then, that the development of recent methodologies as they have been applied in understanding course and outcome have made possible, and mandatory, concurrent recognition of the importance of both the Kraepelinian and Meyerian approaches to understanding the psychoses.

To understand and treat the psychoses, we must try to prevent, or at least reduce, the swing of the pendulum from one approach to the other and to improve our ability to understand and synthesize the psychosocial and the biological, the dynamic and the descriptive, the adaptational and the pathological. This can be done by remaining aware of the dangers inherent in forgetting the importance of both approaches; and, more positively, by developing increasingly accurate methods for evaluating the descriptive and psychodynamic characteristics of such factors as social function, symptomatology, and outcome; and by teaching students about both orientations.

But because we stand on the pendulum, its swing may be difficult to perceive. It is easy to believe that one is taking a balanced

approach but hard to do it. The descriptive-organic approach, on the one hand, stresses history taking, prescription, and advice giving. On the other hand, psychosocial approaches to psychotic patients indicate that more direct personal interaction is important. At its best, the psychosocial approach includes trying to understand, sharing one's feelings, and expressing expectations as means of helping the psychotic return from isolation and dehumanization. A balanced method should include both ways of dealing with patients. Yet few of even the most balanced psychiatric training programs include the two approaches in their teaching.

Although the evidence increasingly points to the importance of both biological and psychosocial factors in the outcome of psychoses, it is easier to talk about a balance between these emphases than to ensure that it exists. Constant attention and review are required.

Psychopathological Aspects of Psychoses: Nongenetic Factors in the Family Setting

Lyman C. Wynne, M.D., Ph.D.

Michael Rutter has commented that the

> . . . importance of the family as a formative influence on a child's personality growth needs no arguing. Particularly in early childhood, it is the matrix within which the child develops, the area where his strongest emotional ties are formed and the background against which his most intense personal life is enacted. The family is the most intimate, one of the most important and most studied of all human groups and yet our knowledge of it remains rudimentary.

In research on the psychoses, the place of the family is fully as significant as it is in the study of other forms of psychological functioning and disorder. Psychoses, with their puzzling derailments of communication and relatedness, generate profound perplexity, disappointment, and fearful self-doubts both in the identified patient and in other members of the family. These disorders strain current family functioning, challenge the merit and meaning of family history, and cast a shadow on generations to come. Compared to the enormous investment in research and treatment on the biological and pharmacological aspects of the psychoses, families, therapists, and researchers alike have tended to evade these painfully human events or only superficially touch their elusive complexities. The central proposition I shall advance here today is that intensified investigation of the nongenetic aspects of functioning in relation to psychotic disorders, especially schizophrenia, should be a very high program priority.

From an etiological perspective, the evidence from genetic studies indicates that, statistically, hereditary factors are contributory to some psychoses but, at the same time, that nongenetic factors must be invoked to account for much of the variance even in "nuclear" schizophrenia. For example, the best recent data suggest that the concordance rate for monozygotic twins is only 25 percent to 40 percent. This means that factors that are not tapped simply by comparing the diagnoses of relatives must be operative in the majority of cases.

Recent adoption studies suggest that although illnesses with characteristics of a broadly defined schizophrenic spectrum occur more frequently in the biological relatives of schizophrenics than in adoptive relatives, the proportion of families in which there is diagnostic concordance is small for typical or process schizophrenia. For example, David Rosenthal, Paul Wender, Seymour Kety, J. Welner, and F. Schulsinger reported that of 36 parents with a clear diagnosis of "chronic" schizophrenia whose offspring were adopted away, only one of the offspring was later diagnosed as schizophrenic (never hospitalized). Only if the diagnostic range is extended into a broad spectrum for both the parents and offspring do their data show significant differences between the index and control groups.

At the same time that the concept of a schizophrenia spectrum is undergoing scrutiny, genetic and nongenetic researchers alike are turning their attention more seriously to family studies in which the transmission of predispositions, rather than psychiatric diagnosis alone, is considered. For example, it has been hypothesized that genetic predispositions to schizophrenia may be manifested in laboratory forms of deviance that differ from clinical assessments of psychopathology. However, methods for the

standardized and reliable assessment of such predispositions are only now beginning to be used systematically.

It should be noted that nongenetic factors, both biological and psychological, may contribute to these predispositions. S. A. Mednick, for example, has suggestive but unconfirmed evidence that birth complications that fall short of causing major neurological damage may contribute to psychophysiological deviance which, in turn, differentiates those high-risk children who become schizophrenic from high-risk children who, so far, do not. Also, he has shown that major factors such as early maternal loss through psychiatric hospitalization modify the actual developmental course of children who are at high genetic risk for schizophrenia.

Although variables such as those described above remain to be demonstrated as conclusively related to schizophrenic illness, it will be much more fruitful if such studies are conducted within the context of family research. Prospective longitudinal studies of children believed to be at high risk for schizophrenia because the child has a schizophrenic parent now include psychophysiological measures of all family members.

Another approach to the family departs from the concept of transmission, whether by genetic mechanisms or by psychological identification processes, of indiivdual parental characteristics to individual offspring. In this alternative view, the patterning and combination of family members into distinctive social units or small social systems are regarded as a crucial phenomenon. Most of the earlier family studies from this vantage point were clinical, involving interviews with family members or observations of families in psychotherapy, beginning after an offspring had already been diagnosed as schizophrenic. Although some of this earlier work mentioned only the impact of parents upon their children, most investigators now explicitly recognize that the processes within the family (or any other special group) are reciprocal. Thus, the behavior and communication of the offspring, including their symptoms, evoke responses from the parents and contribute to the overall family system of communication and relationships. For example, it is quite reasonable to hypothesize that material overprotectiveness could also be part of the mother's efforts to help an offspring who, for example, has minimal brain damage. Intrafamilial attitudes and expectations of this kind are difficult to relate to so-called basic features of schizophrenic illness, particularly the thinking disorders.

Both for this reason and also in order to study observable behavior rather than attitudes or broad personality features of questionable behavioral relevance, a number of researchers have turned to the direct study of family communication patterns. Such studies have indicated that communication behavior in the families of schizophrenics does differ from that in other families. By and large, the trend of recent work has been to spell out hypotheses derived from earlier clinical formulations, but, because of the complexity of the variables, no single experiment or sample can be expected to test the clinical formulations. Rather, long-term research involving the development of improved methods for the study of specific variables is the approach that is necessary and under way.

Traditionally, schizophrenia has been regarded as a disorder of individual persons or as a still more localized pathological process to be found within the brain. The difficulties of reliably assessing psychopathology, especially so-called "typical" schizophrenic symptomatology, have already been mentioned above. Such difficulties of adequate diagnostic evaluation are serious even when traditional definitions of the concept of schizophrenia are used.

However, a further complication in more recent family research is that many family researchers and therapists now prefer to define schizophrenic illness as a disorder of relationships between persons and not one within any individual person. Using this kind of conceptualization, dysfunction begins with disturbed relatedness and communication in family life; it later may be replicated in relationships outside of the family, both with persons in the community and with psychiatrists as well. In this view, the disorder cannot be appropriately localized in any particular family member. However, if the role defini-

tions given to a particular family member become stabilized, e.g., through scapegoating processes, and if these family definitions are reaffirmed by professional persons with special knowledge and authority, then the prevailing tendency to localize the disorder in a single family member becomes both intelligible and socially functional.

In this view, "madness" then becomes another form of deviance comparable to criminality, with fixed definitions that often disqualify the individual from full recovery and rehabilitation. "Labeling theory" is an attempt to describe social processes that stabilize and segregate persons who have been identified as schizophrenic or as chronically mentally ill. Although it is inappropriate to interpret such a theory as etiological, one can nevertheless recognize a growing body of clinical, experimental evidence that social groups (including families) do develop regulatory processes that tend to maintain an equilibrium which may well interfere with symptomatic recovery and contribute to chronicity.

Clinical evidence that re-equilibration of the family disrupted by acute psychosis can be quickly regained is suggested by family crisis-intervention treatment programs. D. G. Langsley and D. Kaplan have shown that intervention with families at time of crisis, which forestalls enduring role assignments of a member as "the sick one," reduces the need for hospitalization of the identified patient in a remarkably high proportion of cases.

Recent WHO research suggests that schizophrenics in some underdeveloped cultures do not appear to become chronic as regularly as those who are treated in European and American hospital settings. The implications for programs of prevention and treatment are clearly substantial and, once again, are not at odds with the concept of genetic vulnerability as a contributing etiological factor.

As an alternative to the traditional individual starting point for conceptualizing schizophrenia, one can begin with a clinical classification of family relationships. Also, a classification of families has been experimentally derived and is distinct from individual diagnostic categories.

The separate assessment of family and individual variables permits the formulation of testable hypotheses about the connections between individual and family levels of functioning. However, with the classification of families still in an exploratory stage, most of the family research thus far has used diagnosis of a single member of a family as the criterion for identifying families for study. Thus far, there have been relatively few experimental studies of families in which an offspring has become ill later in life. This has led to a neglect of families of the well-organized, paranoid schizophrenics and manic-depressives whose age of onset of symptomatology is typically later than that for acutely disorganized schizophrenics.

Further work is needed to show which aspects of family life are relevant to schizophrenia and influenced by social and cultural variables. A suggestive study has shown that communicational features associated with lower-class social status are not the same as the problems found in the communication of the families of schizophrenics. Also we have found that in a large sample of disturbed families, the parental communication behavior is not significantly related to social class, but the very lowest social stratum has not yet been extensively studied in the family communication research with these methods.

NIMH collaborative studies with Japanese colleagues suggest that the communication deviances found in American families of schizophrenics are also found in Japanese families of schizophrenics. However, some categories of communication deviances are more prominent in the one culture than in the other. This also seems to be true in a comparison of English and American family data.

Another related issue concerns the difficulty of taking into account important relationships of persons who have been parent surrogates—older siblings as well as foster parents and members of the extended family. In some cultures and social class groups, these variations from the simple nuclear family are obviously crucial to understanding the nature of the learning experience of the

growing child. Indeed, such factors are probably important even where the nuclear family is especially prominent, as in recent American culture. It should be obvious that the family is by no means the only social organization that needs to be studied in relation to schizophrenic and other psychopathological outcomes.

There have been two main alternative strategies for data collection in studies of family communication. First, some studies have called for the examination of communication behavior of family members other than the identified patient; these investigations have included hypotheses about the impact of parents upon an offspring growing up with them. Second, the entire family, or at least the parents and the identified patient-offspring, are studied in direct interaction and communication with one another. The first strategy is based upon the hypothesis that enduring patterns of behavior can be sampled and that certain features of parental communication are stylistically or formally similar from one situation to another; the second approach is more concerned with the immediate situational aspects of direct family communication that may or may not be part of an enduring pattern.

In our use of the first of these approaches, Margaret Singer and I successfully predicted from certain communication features found in parental Rorschachs what the diagnostic characteristics of the most disturbed offspring in a family would be; we also matched successfully the Rorschachs of the index offspring with the parents of the same family.

The concepts underlying this work made use of the formulation that the way persons go about sharing foci of attention and derive meaning from external stimuli such as inkblots is related to the form of their thinking. During growth and development, this learning experience could, it is hypothesized, contribute to disturbed thinking and communication of children who are trying to relate to these parents.

Later, we spelled out a series of 41 specific categories of behavior believed to be especially frequent in the parents of schizophrenics and which could be reliably identified in verbatim Rorschach records. Still more recently, we have found that specific categories of these communication deviances are especially frequent in the parents of schizophrenics and significantly differentiate them from the parents of borderline and neurotic patients and normal subjects. Although parental communication deviance and parental psychopathology are conceptually linked and are statistically correlated to some degree, they can be differentiated both conceptually and statistically. That is, communication deviance scores and psychopathology ratings overlap but are by no means identical.

Out of a series of 114 families, high communication deviance scores not only correctly identified all 20 parental pairs in which one or both parents had borderline psychopathology or worse, but also correctly identified all 24 additional parental pairs who had a schizophrenic offspring, even though no parent had a schizophrenic illness or a borderline syndrome.

Along with J. Bartko and M. Toohey, I examined counteractive or corrective family factors that might have forestalled a schizophrenic outcome when one parent is borderline or schizophrenic or had many communication deviances without formal psychiatric diagnosis. If the well spouse showed active, corrective features, we predicted that an offspring was not likely to become schizophrenic, though a less severe personality disorder or neurosis may have developed. When paired with a well spouse who was passive or inactive, the offspring of an equally disturbed parent was correctly predicted to be schizophrenic. Thus, even though the family members in this research were tested individually, a family-system hypothesis was used and supported by these findings.

This method of studying parental communication has now also been applied to Rorschach records from an Adoptive Parent Study conducted in Bethesda by Wender, Rosenthal, and Kety. Using global clinical ratings of severity of parental psychopathology, Wender et al. previously reported support for a genetic hypothesis. More recently, these same parents have been studied with blind, reliable ratings of communication de-

viances in the verbatim transcripts of their tape-recorded Rorschach records. This approach strongly supports a psychosocial (experiential) hypothesis: The adoptive parents who had reared a schizophrenic offspring were indistinguishable from the comparison group of biological parents who had reared a schizophrenic offspring, and the mean frequency of communication deviances in each of these groups was significantly higher than that in the adoptive parents of nonschizophrenics. Because different measures were used by Wender's group and my own, the results are complementary, providing support for both genetic and experiential contributions to schizophrenia.

In addition to the study of family members in individual test situations, a large and diverse group of studies has been carried out in which the family members are studied in communication with one another. These methods have been reviewed and evaluated by J. M. Riskin and E. E. Faunce. Conjoint family therapy excerpts have been successfully used as one means of sampling family communication. However, standardization of procedures is more easily achieved by presenting families with a variety of specific tasks, such as the discussion of alternative perceptions and interpretations of Rorschach or TAT cards, and conjoint problemsolving tasks. Such methods permit a large number of variables, such as acknowledgment and task-focusing, to be studied objectively and systematically, with comparisons between families as total units, between subsystems of families (such as the marital dyad), and between individual roles within families. These procedures are now being used both with the families of normals and psychiatrically disturbed schizophrenic and nonschizophrenic patients. The further application of these experimental methods to schizophrenia and family research will help clarify the significance of a multitude of variables which previously could be studied only impressionistically. It should be noted that the findings emerging from these studies cannot be deduced from the psychological or biological characteristics of individual family members.

The concept of families as transacting social units means that direction of effects can be multiple, but it does not rule out the possibility that the participation of certain family members may be more fixed than that of others. Neither can there be any assumptions about the sequential order in which these patterns of transacting originated. Therefore, family researchers have been seeking ways in which developmental sequences leading to diagnosed schizophrenic illness can be untangled. As I have indicated above, a partial approach to this question is to evaluate family members with measures for which other evidence suggests that levels of functioning are likely to be enduringly stable—and likely to antedate the onset of symptomatic illness in any family members. Some of the response dispositions and some of the formal communication patterns that have been discussed above may qualify as such variables. However, further longitudinal research evaluating their stability over time needs to be carried out.

Another approach is to study families with more than one offspring and to compare family patterns, particularly parental responsiveness, when a symptomatically disturbed offspring and a well sibling are present. It has been hypothesized that if parents behave without deviance to a normal offspring but are deviant in response to a disturbed offspring, then their behavior might be regarded as responsive rather than causative of the offspring's disturbance. A study of intrafamily differences, comparing having the patient present versus having the siblings present, showed that many families and parents alter their interaction patterns with one offspring compared to the other but not consistently so in relation to the offspring's diagnosis. Such inconsistency is expectable in the light of numerous clinical observations made from the family system viewpoint, because diagnosis of offspring is only one of numerous variables producing role differences between siblings.

The meaningfulness of each variable must be examined in the light of the developmental history of the family and the children. For example, in some families, relatively trivial or intrinsically unimportant differences between the offspring, such as birth order or

degree of shyness or talkativeness, affect the particular kinds of roles allocated to the various offspring. Later, one family member may become the repository of an overt disorder and may be a scapegoat in the family. Such scapegoating may help the family continue to function as a unit in the face of difficulties that would be disorganizing and disruptive of other role functions if it were acknowledged that other family members also behaved in irrational ways at times. However, there is no reason to expect consistent sibling differences related to a particular diagnosis. Therefore, the study of sibling differences is important in understanding family dynamics but is an inadequate method for studying direction of effects between parents and offspring.

N. E. Waxler suggested the construction of "artificial" families as an alternative for studying the sequences in which individual and family disorders precede or follow one anothe . For example, the interaction of a child with someone else's parents, and vice versa, is studied. However, it appears farfetched to infer causality by comparing the impact and learning experience in a brief experimental session with the effects of interactional patterns evolving in stages from the earliest formative years of the offspring.

Certain kinds of questions about the direction of effects are not likely to be satisfactorily answered until prospective longitudinal studies are conducted. Such studies are subject to multiple methodological pitfalls but are now more practical than in the past for three reasons. First, more detailed hypotheses are now possible about what kinds of variables should be studied in families prior to the onset of symptomatic illness in any family member. Psychophysiological and communication data are examples of the kinds of variables with predictive value that now can be included from the beginning of such studies. Although clinical case records are useful, more systematic measures from laboratory and psychological testing procedures should be added.

Second, by comparing high-risk with low-risk samples, more economical sampling is possible in longitudinal research. Obviously, with an incidence of schizophrenia of about 1 percent in the general population, it is not feasible to study large samples comprehensively in predictive longitudinal studies unless preliminary screening is carried out, preferably with the identification of high-risk versus low-risk categories of subjects. Families of children of schizophrenic mothers and of disturbed but not yet schizophrenic adolescents are especially strategic high-risk samples.

Third, the use of accelerated longitudinal methods, as suggested by R. Q. Bell some years ago, may make such studies pay off in a more reasonable length of time than was possible in earlier 30-year longitudinal studies. A high-risk study assessing the accelerated longitudinal method is now under way at the University of Rochester. With a convergence design, samples of subjects over different age ranges can be studied simultaneously. For example, a 5-year study with five groups of subjects—from birth to age 5, from 10 to 15, from 15 to 20, and from 20 to 25—is more feasible than to study an equal number of subjects all beginning at birth through age 25. In principle, data about this broader age span can be obtained with proper statistical sampling in this accelerated longitudinal approach.

Developmental psychology and its methods thus are now being linked to family research and these, in turn, to hypotheses about factors that lead to diagnosable schizophrenic illness. Such work is now getting under way or is being planned for the near future. However, this was not possible until substantial cross-sectional family research had been carried out. These cross-sectional methods and findings are now being applied in the longitudinal and high-risk family studies.

Finally, in examining nongenetic factors, we are drawn to a renewed respect for the health-promoting functions of family life. Compared to what might be expected on genetic grounds, there appears to be an attenuation of disturbed behavior in most families. For example, only 10 percent of schizophrenic parents have an offspring with a schizophrenic disorder. There is no simple or consistent connection between episodic

symptomatic disorders of parents and the psychiatric outcome of their offspring. However, there appear to be predictable links between recurrent patterns of family life and the functioning of individual family members. These family patterns deserve intensified systematic research into those features that have possible pathogenic significance and those with health-promoting potentialities. Studies of the latter provide clues for clinical strategies for both prevention and treatment. We have much to learn from families who have successfully weathered chronic stress or multiple crises. Most family therapists of the present focus on efforts to help families build upon their existing strengths, which have far too often been little appreciated by the families themselves and pathology-oriented diagnosticians. To paraphrase Harry Stack Sullivan, our families are, after all, far more simply healthy and human than otherwise.

V. EPIDEMIOLOGICAL AND SOCIAL FACTORS IN PSYCHOSES

The growing appreciation of the role of biology in mental illness should not obscure the equally important part that psychosocial factors play. As knowledge about mental disorder has increased—and the advances have been significant in the past 25 years—so has our recognition that biological and psychosocial influences interact in psychosis in extremely complex ways. If we were once inclined to be overly optimistic about finding solutions easily or quickly, we are less naive now. The future poses many problems, both theoretical and practical, which will call upon the widest possible range of skills in biological and social research. What is needed, as most researchers recognize, is a melding between the psychosocial and the biogenetic approaches to problemsolving. Whatever dichotomy exists between the two is a dichotomy of convenience only; any real understanding of the serious mental disorders must necessarily encompass both points of view. It must also take into account what the epidemiologists have documented: The psychoses remain among the Nation's most urgent, unsolved health problems.

James A. Goodman, Ph.D.

Social Factors Affecting Psychotic Behavior

David Mechanic, Ph.D.

Considerable progress has been made in the care of psychotic patients in the past two decades. However, much of it has been due more to changing social definitions and practices than to any new understanding of psychotic behavior. We have learned that there are no simple and easy solutions; progress in the care of psychosis requires basic knowledge that still eludes us, and, as a result, our approaches to management of patients are difficult and costly. Much of the thinking of the 1960's, however useful in mobilizing public opinion and widespread support for mental health efforts, was simple minded and over optimistic. The danger now is that we will enter a cycle in which naive optimism is followed by excessive pessimism and by the dangerous myth that progress is impossible without biological breakthroughs.

Despite the confusion of the 1960's, some useful advances were made in the frames of reference for viewing psychotic behavior and its more effective management. An awareness that psychotic disorders are not simply a more serious manifestation of commonly occurring distress and impairment, but rather appear to have distinctive natural histories and epidemiological pictures, is a major condition for further progress.

Increasingly, we are moving from the notion that a standard therapy fits a variety of mental disorders to more careful description; we are now searching for more targeted interventions. As a matter of public policy, mental patient care has moved from dependence on hospital settings to a variety of community care situations. At the same time, we have been confronted by the realization that administrative policies are not a substitute for adequate knowledge of the cause or course of mental disorder. While informed and humane administrative policies are a prerequisite for a sound mental health approach, such an approach depends on better understanding of etiology of specific disorders and their outcomes in varying environments and treatment settings.

It is useful to review some of the valuable results of the ideological ferment of the past 20 years. It led to the realization that whatever genetic and neurobiological factors are involved in the causation of the psychoses, they interact in very complex ways with social and cultural factors. The manifestations of the disease process are a product of these interactions. Whatever the predispositions, they may be exacerbated or contained by the manner in which psychotic patients are defined and managed and by the nature of the social environment in which they live. The new biological psychiatrist should never again make the mistake of his predecessors in assuming that because psychotic states have important hereditary and biological foundations, the structure of treatment and supportive environments are unimportant.

The ideological debate on the nature of mental disorder so debased the use of psychiatric concepts that there is now a new awareness of the need to avoid both a glib disease perspective and a crude social labeling. Efforts are being made to define concepts more carefully and to improve the classification of psychiatric phenomena. As long as the concept of schizophrenia, for example, was used to refer to everything, it meant nothing. Both the collaborative American-British study and the cross-national WHO study illustrated the value of being more careful in describing mental illness.

From the perspective of mental health care administration, the turmoil of the 1960's has

given us all a renewed appreciation of the civil rights of the mentally ill and the dangers of the self-fulfilling prophecy. With the shift to community care we have again come to appreciate the disservice professionals can do to the patient under the guise of treatment when they engage in excessive restrictions and foster dependency. It is now more difficult than it once was to confuse custodialism for the purpose of community comfort with effective treatment efforts.

We are also learning that changing our concepts, and even our administrative procedures, is inadequate for the real demands of effectively managing psychotic patients. Community care without sustained programs and followup support is an invitation to a new type of erosion of human potential, except that now it occurs in a community and not in a custodial institution. Realities are forcing a reconsideration of the appropriate role of mental hospital care in the entire spectrum of services and a rethinking of the concept of dangerousness. We must consider how we can make better predictions than at present and take a more realistic view of both the benefits and the cost of alternative means of managing psychotic patients.

Despite these lessons, prudence requires that we recognize the imprecision and uncertainty of our understanding and that we be aware that we still lack specific guidelines for organizing environments to sustain psychotic patients in the community. We have not yet adequately learned how to balance or even measure the social costs for the community against the ideology of community care. Despite much rhetoric, we continue to have difficulty in maintaining the supportive network of services. This problem arises in part because of funding problems; in part because of the difficulty in continuing a sense of innovation and momentum in the care for chronic patients, which is a frustrating task; in part because of the difficulty in coping with reactions and pressures of communities who accept the idea of community care, but in other people's communities; and in part because we often do not know what we are doing or how to do it.

The difficulty in organizing professionals for providing long-term care to chronic patients should not be underestimated. Developing programs for such patients is always difficult and frustrating, and it involves activities that are not particularly likely to bring prestige and recognition. Professionals often lack the skills necessary for political implementation or for dealing with numerous problems of community resistance and funding. It is easier to resort to more comfortable patterns of work then to persist in the face of recalcitrant communities and intractable disorders. While we can talk about the need for changes in psychiatric education and changing the status and rewards of different kinds of professional work, and the challenge of caring for chronic psychiatric illness, we kid ourselves if we think this is any more than reformist rhetoric.

Major changes in the professional stances of the relevant professions will depend either upon a major advance that can be applied without too much disruption in ongoing organization, or upon how services for mental disorders are paid for and who will be eligible for payment. One of the adverse consequences of the expansion of mental health concepts in the 1960's was the redirection of attention away from the needs of the psychotic patient. If large proportions of the community were mentally impaired, as some studies suggested, and if such impairments were only a precursor of more severe pathology, then it seemed less compelling to devote large resources to the few who suffered from chronic psychiatric illness. Instead, it seemed reasonable to devote attention to moderate disabilities before they became severe. Community mental health centers had diffuse missions and found it easier to focus on assistance for those with less severe disorders. The major difficulty was that the theory of preventive psychiatry was more rhetoric than substance.

As we move toward National Health Insurance in the coming years, the manner in which psychiatric benefits are defined in this program is likely to have an important effect on how psychiatric personnel will spend their time and how much attention will be devoted to psychotic patients. It is apparent that various interest groups are active in seeking to influence the definition of those benefits.

Maintenance of parallel systems of medical and mental health services, as they are now organized, will reinforce a tendency to neglect the problems of the less attractive, more chronic patients. Mental health services for more ordinary problems of living ought not to be categorically organized or financed. There is, however, a need for categorical services in the mental health service sector, and such financing should be targeted, specifically, for the care of the chronic psychotic patients and others with similarly severe conditions.

Developing better programs of intervention depends on continuing research programs. Not only must we understand the genetic biochemical and environmental factors contributing to psychoses, but we must also develop a more adequate grasp of the intervening variables that help explain why some people with genetic predispositions actually develop psychoses while others do not. Why do some children of two mentally ill parents or schizophrenic parents do so badly while others not only achieve adequate adjustment, but appear to cope admirably? Why do some children at an early age appear to have self-limited conditions, while others enter on a trajectory of one disaster after another? Some studies by Lee Robins and others have documented the devastating and discouraging course of behavior disorder problems in childhood. One of the great challenges of epidemiological study is to better understand the processes of such disorders and how we might successfully intervene.

In approaching these problems, I emphasize psychosocial aspects. Naturally the biochemical and neurobiological mechanisms are important. Moreover, the interactions among variables in these disorders are sufficiently complex so that it is increasingly obvious that the competence of any one discipline is not fully satisfactory. Interdisciplinary work has pitfalls, but it is essential if we are to explore some of the interactions that are central to the process of psychotic behavior.

A major difficulty is methodological. We lack effective ways of measuring adaptive capacities and the role of adaptive mechanisms in ameliorating or short circuiting environmental threats or biological propensities. Yet, despite these problems, there is growing realization that these intervening processes are central and that even extreme stress evokes a variety of responses and varying levels of harm in populations exposed to it. Fortunately, there has been a slow accumulation of results that, while not definitive, illustrate the importance of these intervening processes. One study, for example, involved the careful observation of family interaction where there was a schizophrenic patient. Intense interaction was found to be associated with the recurrence of schizophrenic episodes, in contrast to a family climate that was less intense and more detached.

This kind of information is consistent with clinical impressions and could be helpful in making community living arrangements for schizophrenic patients. To take another example, George W. Brown and J. L. P. Birley found that significant life changes occur far more frequently prior to the onset of acute schizophrenia than in normal controls. Such events were associated with the building up of tension that preceded the acute episode. While such information may not necessarily give us the knowledge to control the occurrence of such life changes, it may provide opportunities to diminish their consequences.

In short, understanding the role of environmental stress in disease, or the disruption of behavior, and how to retard its effects requires that we understand the intervening variables and how they either protect the person from assault or speed the dissolution of effective adaptation.

It is useful to consider five types of deficiencies affecting the disruption of effective behavior. This classification may be a useful way to organize our thinking about the intervening processes and may also be useful in designing services for psychotic patients.

1. *Material resources.* A major impediment to effective social functioning is the lack of material resources necessary to sustain the social group. While the link between poverty and illness is certainly not direct, it contributes to the problems of adaptation among vulnerable persons and increases the probability of disorganized behavior. M.

Brenner, for example, has found that economic recessions are followed by increased admissions to mental hospitals, and he makes a reasonable case that these correlations are not easily explained simply as a result of changing definitions of disorder under changing economic conditions.

At the most primitive level, the adequacy of nutrition and shelter is central. Inadequate nutrition in particular is linked to a vulnerability and increased mortality resulting from disease, and affects both social and intellectual development. With reference specifically to psychotic patients, there are continuing indications of gross deficiencies in the material environment necessary for a minimal standard of living quality. As communities have mounted political pressures to resist board and care facilities, halfway houses, and outpatient facilities, mental health departments have often followed the line of least resistance, locating such facilities in the most ecologically disorganized areas of cities. Patients in such areas suffer high risk of victimization and may further be exposed to the anomie and hopelessness that frequently pervade these environments.

2. *Lack of appropriate skills.* The adequacy of any social group or of individuals depends on the effectiveness of cultural preparation and the availability of problemsolving tools necessary to deal with their environment. What may be an ordinary situation to those with skills or otherwise adequate cultural preparation is a crisis for those who lack them. As care for psychotic patients has increasingly been provided in community contexts, it has become more apparent how frequently such patients lack basic skills essential to everyday living. While the problem of the psychosis extends well beyond inadequacies of skills and cultural preparation, the absence of these skills, or their erosion due to the chronic course of the illness, exacerbates the problems of such patients in the community. It makes it more difficult for them to find and maintain employment, to establish functional interpersonal relationships, to enjoy adequate living quarters, and to avoid difficulties with the authorities. Moreover, the dependency of chronic psychotic patients means that they are likely to have continuing contacts with official bureaucracies, and skills in handling these become important for their satisfactory community adjustment.

Some efforts have been made to assist chronic schizophrenics in improving everyday skills on the assumption that these contribute not only to more adequate social functioning, but also help avoid repeated rehospitalizations. While the evidence is not all in, there are some indications that this approach facilitates more effective community performance, at least in the short run.

Speaking more generally, there is a growing body of evidence suggesting that the movement of populations from one environment to another, such as from rural to industrial life or from country to city, is associated with a higher prevalence of disease of a variety of kinds. Perhaps the groups least well fitted for major social and cultural change, but subjected to it as a matter of course, are chronic psychotic patients who increasingly reside in unfamiliar settings with limited social supports.

Although we still lack definitive evidence that simple skills contribute to a more favorable course in the progression of psychosis, it would seem useful to give this area greater emphasis than at present and to make serious efforts to evaluate their effects and their cost-effectiveness.

3. *Lack of adequate defenses.* Man's ability to engage in effective behavior depends not only on constitution and past preparation, but also on psychological capacities to deal with signals of danger and hopelessness. Cultural devices must be available for a person to contain and control feelings that hamper long-term adaptations and to facilitate continued attention to ordinary activities rather than to flight.

I have already referred to some of the evidence that schizophrenic patients have difficulties in dealing with intense personal relationships, for whatever reason, and that patients vulnerable to depression appear to be unusually susceptible to situations in which they suffer a sense of loss. Building stronger personal defenses is perhaps the most difficult aspect of improving adaptation, yet this is the area where traditional psy-

chiatry and psychoanalysis have devoted their greatest emphasis. We do not have good evidence that we can successfully alter the defensive processes of psychotic patients even when great effort is devoted to this task. Perhaps a more effective route is through building social supports.

Here an analogy from the accident field is instructive. Health education programs have thus far found it relatively futile to try to alter significantly the incidence of automobile accidents through attempts to modify driving behavior. However, we know that technological and legal factors such as seatbelts, highway construction, auto design, and speed limits have very significant effects on the occurrence of fatalities. If there is a technological side to the treatment of the psychoses, it lies in how we socially organize the provision and monitoring of drug use, and the efforts we make to develop viable services and social support.

4. *Lack of adequate social supports.* It is a truism that men are interdependent and that successful functioning depends on the material assistance and emotional support we receive from our fellows. The absence of such supports makes people vulnerable to interpersonal and environmental assaults and a variety of other adversities. Often just the knowledge that help is accessible gives people the confidence to cope. But in times of difficulty we depend very heavily on the assistance of others. Such supports are frequently unavailable to psychotic patients in the community.

First, such patients often have difficulty in close personal relationships with others. Second, over the course of time, their bizarre behavior and life difficulties often result in the alienation of family and significant others. Third, such patients often fail to maintain contact with services unless the pattern of services is well organized and aggressive. Thus, chronic psychotics are not only likely to lack such supports, but they also are least likely to seek them out. Although psychoactive drugs are important in the community maintenance of chronic psychotic patients, these patients often fail to maintain their drug therapy and often stop using drugs when their psychological states are most tenuous. Without well-organized and aggressive services, such patients are often lost in the community and eventually end up in difficulty. Thus far, we have had severe problems in developing and maintaining well-organized patterns of supportive care.

5. *Sustained motivation.* Social adaptation depends on a continuing willingness to remain committed to ongoing social activities. While withdrawal is a natural and often an effective means of reducing a sense of threat in the short run, it becomes maladaptive if it persists as a continuing pattern. As people deal with problems by withdrawing, their skills and social contacts tend to erode and they eventually develop a sense of hopelessness.

One of the things we have learned very well in the care of psychotic patients is that withdrawal and inactivity lead to an erosion of a patient's capacity to continue and regain important social roles. The specific activity of the patient seems less important than his remaining actively involved, in contact with other people, and constrained in some degree by social expectations. While we have a difficult time unraveling cause from effect, clearly, for such patients, structure involving some demands, without taxing their ability to conform, contributes to a higher level of social functioning.

In sum, I believe that these five areas of programing—material resources, skills, defenses, social supports, and sustained motivation—provide a perspective that makes clear some of the challenges facing us in the coming years. These challenges exist in research as well as in designing services. We must develop better understanding of the important interactions in the progression of psychosis and better strategies for helping the unfortunate patients who cannot wait for us to learn all there is to know.

Epidemiology and the Planning of Services for the Mentally Ill

Ernest Gruenberg, M.D., Dr.P.H.

The public health mission is to organize activities which lower the prevalence of disease and disability by preventing those conditions which are preventable, determining those conditions which can be cured, and mitigating the disability of those people who develop unpreventable and incurable illnesses. These activities are carried out by applying rehabilitation and by preventing disease and disability. The operating programs put our techniques to work in an organized way. Our research programs need to focus on the gaps in techniques and on the problems which remain to be solved.

The epidemiologist makes a contribution to the research for preventable causes. He makes another contribution by taking stock and estimating what these techniques could accomplish if fully applied and by estimating what has been accomplished and pointing out what needs to be done in the future. We have tried to provide the health movement with a sense of accomplishment, direction, and, on some occasions, a sensation of specific failures. The failures of the recent past are the tasks of the future.

Prevention of premature death has been the preoccupation of public health for over 100 years. The time comes when the prevention of premature death can raise the prevalence of disease, and that is what is happening in the United States today. The postponement of death during the last eight decades has increased the prevalence of the severe mental disorders.

For example, 4 or 5 years ago, pneumonia was a serious problem for clinical medicine. It was a major cause of death which affected all age groups. Recovery was rare. In time, an amazing technology reduced the mortality rate from pneumonia.

But pneumonia had been known in clinical medicine as the "old man's friend" because it was the most common way by which lingering and terminal illness was quickly ended. It was a relatively painless blessing to those who were confused and weak and helpless because of senile brain disease. Now the old person who develops a low-grade fever is given antibacterial medication. The fever subsides and the chronic illness lingers on. This happens repeatedly until some drug-resistant infection takes over or something else intervenes. Chronic brain syndromes rarely kill directly. The average duration of senile brain disease psychosis has stretched from under 3 years to something closer to 6 to 10 years.

The rising occupancy rate in nursing homes has been attributed to the indifference of families, breakup of family solidarity, and so forth. There is little good evidence that these are the key factors. People still make enormous sacrifices. But the burden that is readily tolerated by a family for a few months or a year becomes very heavy when it lasts for a few years and impossible when it lasts a decade.

I have been seeking to find data which tell us how fast the prevalence of severe mental disorder has been rising among the aged. However, one associate asked me to help him figure out why one carefully studied small population showed higher prevalence rates in 1957 than it had in 1947. As far as I know, this small community in the south Swedish countryside is the only example in the world of an entire population which was carefully studied for all mental disorders at

two different times. These data belong to Professor Olle Hagnell, University of Lund, Sweden, who has kindly permitted me to report them.

In the 70- to 80-year-old age group the prevalence rate has trebled from 1947 to 1957. In women the rate rose from less than 3 percent to 21 percent of all women in their 70's. In women the mortality rate dropped both for the sick and the well, but more for the sick than for the well. I estimate that in the past 20 years the average duration of an episode of mental illness terminated by death in women rose from 4 to over 12 years.

But in men in their 70's, improved life expectancy was found only among those with brain syndromes. There was no change in mortality rates for men who had been diagnosed as having no mental disorder. The life expectancy of the sick rose during that decade, but it is still much, much higher for people with mental disorders than for the rest of the population.

This effect is so marked in this small population that the overall age-specific death rate for men rose between 1957 and 1962. Judging from the findings of this small population, there is disproportionate postponement of death among the elderly sick, that is, people with chronic brain syndrome.

From 1947 to 1957, the general improvement in life expectancy was disproportionately an extension of the lives of mentally sick people; for people who do not have any evidence of mental disorder, the improvement is much less. This is because death-delaying devices are postponing death for people with chronic brain syndromes much more than they are for those without such syndromes.

The same principle applies at the other end of life. The advances in pediatrics and obstetrics are disproportionately saving the lives of brain-damaged children as compared to non-brain-damaged children. This is very dramatically demonstrated in mongolism. Forty years ago, a mongoloid newborn had little chance of living beyond 4 years of age. Most of them now live beyond 30 years of age.

I know of no efforts to plan for increased services either to the brain-damaged infant or adult based on these well-established facts. I know of no program to organize and provide services to the mentally ill among the aged to take account of their increasing prevalence rates.

It would be easy to say that research on the preventable causes of senile brain diseases and other brain diseases is about to enter a golden age. I think that is a possibility. But if society can systematically watch the rates of such disorders rise and fail to plan to increase services for them, I wonder if it will have the good judgment to place the search for preventable causes at the high priority it deserves.

Psychiatric Services and the Changing Institutional Scene

Morton Kramer, Sc.D.

Important changes have taken place since 1950 in the numbers and characteristics of persons in mental hospitals, in the locus of delivery of mental health services, and in the volume of services provided in different types of psychiatric facilities. Many of these changes were brought about by the application of knowledge gained from research on the etiology, treatment, and rehabilitation of patients with psychoses and other mental disorders. Federal legislation, such as the National Mental Health Act, Community Mental Health Center legislation, and similar acts passed by State legislatures, have played a major role in stimulating and supporting the research that yielded this knowledge and developing service delivery programs for its application. Other changes have resulted from population growth, social developments since 1950, and advances in clinical medicine.

In 1955, after 100 years of steady growth, the population of the Nation's State mental hospitals began to decline. In that year, the inpatient services of these hospitals accounted for 818,832 patient-care episodes, or 505 per 100,000 population. By 1973, the number of inpatient care episodes occurring at State mental hospitals decreased to 651,857, a rate of 313 per 100,000. These decreases were a direct result of the strong development of community mental health programs designed to place long-term, chronic patients in alternative facilities or to return them to the community. Such programs diverted considerable numbers of people, particularly the aged, to nursing homes. In 1963, for example, 47 percent of persons 65 years and over with a mental disorder were in mental hospitals, and 53 percent in nursing homes. By 1969, the corresponding proportions were 25 percent and 75 percent, respectively. Institutionalization for such mental disorders as schizophrenia and affective disorder was also reduced, largely because of improved treatment by pharmacology.

At the same time, a number of factors have operated to increase the populations of some other institutions. Improved medical care, health, and social services have prolonged lives and, by so doing, have produced a large population of persons with chronic illnesses and disabling conditions who require long-term care in nursing homes, homes for the aged and dependent, and chronic disease hospitals. Between 1950 and 1970, there was an increase of 133 percent in the population of homes for the aged and dependent.

The coming of age of children born during the post-World War II baby boom has also had its impact. By 1975, these children became 18-25 years of age, an age group in which the incidence of some conditions leading to institutionalization is high. It is, for example, a high-risk age group for schizophrenia, a mental disorder frequently requiring admission to a mental hospital. It is also a high-risk group for arrests for crimes of violence, burglary, and other offenses that may lead to prison sentences. Social problems, too, such as poverty, unemployment, broken homes, and delinquency, have increased institutional populations in training schools, detention homes, and various correctional institutions. From 1950 to 1970, there was an increase of 38 percent in the resident rate of training schools for juvenile

delinquents, and of 11 percent in homes and schools for the mentally handicapped.

The trends of 1950 to 1970, when related to expected population trends in the United States for the next decade, give some insight into mental health services needs in the near future. There can be little doubt that such needs will increase. By 1985, the population of the United States will have grown to about 241.7 million people, about 19 percent greater than in 1970. The largest increases will occur in age groups known to be characterized by consistently high admission rates to psychiatric facilities, correctional institutions, training schools, homes for the aged and dependent, and homes and schools for the mentally handicapped. If we assume, for example, that the annual incidence rate for schizophrenia will be the same in 1985 as in 1970, then we can expect 183,808 new cases of schizophrenia in 1985—an increase of 25.2 percent. Even if a major research breakthrough should occur, the likelihood of achieving significant reductions in new cases of schizophrenia would be small in view of the large increases expected in the populations at high risk for this disorder. It would require very efficient methods of prevention indeed to counterbalance the increases in numbers of new cases that can be expected as a result of population increases. The same reasoning applies to the occurrence of new cases of affective disorders, brain syndromes, neuroses, and personality disorders.

The prevalence of mental disorders will increase in the coming years, both because of population increases, especially in high-risk age groups, and because of increased longevity. Advances in clinical medicine have postponed death for many. Lifesaving and life-prolonging procedures have produced a sizable population of persons with chronic illnesses, many of them with associated psychiatric and psychosocial problems. Further, mortality rates among the mentally ill have been reduced, resulting in greater numbers of mentally ill persons in the population.

Overall, then, current data and trends indicate the dimensions of some of the problems for mental health care in the immediate future. These problems present a continuing challenge to researchers in all of the sciences involved in unraveling the causes of mental disorder and in improving treatment and rehabilitation of mental patients.

The challenge is especially great for those of us who are responsible for the development of the statistical and epidemiological services essential to the collection of data needed to meet the requirements of the Community Mental Health Centers legislation. Despite progress in epidemiological and biostatistical research on mental disorder, there is still an agenda of considerable unfinished business. We are aware of gaps in our knowledge concerning the distribution of mental disorders, the patterns of use of mental health and related human services, and their effectiveness.

In our attempts to fill these gaps, high priority should be given to the development of generally applicable procedures for case finding, improved diagnostic methods, more precise measures of need for specific kinds of psychiatric services, followup studies, classifications of psychosocial factors, and social indicators. Solutions to these problems will greatly help to narrow the gap between knowledge now available and knowledge needed to fulfill our mission.

Of particular importance for epidemiological research is the establishment of several field research units with adequate staffing and stable, long-term financing. These units would design and implement research to determine the extent to which community mental health programs are affecting the level of disability from mental disorders. Indeed, it is a matter of the greatest urgency that adequate resources—financial, scientific, and administrative—be made available to solve the problems discussed here. As we approach future demands on mental health services, it is imperative that we be able to assess and document the effectiveness of programs to prevent and control mental disorders.

☆ U.S. GOVERNMENT PRINTING OFFICE : 1977 O—242-844